

SCIENCE

Vol. 91

FRIDAY, MAY 24, 1940

No. 2369

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SCIENCE: A Weekly Journal devoted to the Advancement of Science, edited by J. McKEEN CATTELL and published every Friday by

THE SCIENCE PRESS

New York City: Grand Central Terminal

Lancaster, Pa.

Garrison, N. Y.

Annual Subscription, \$6.00

Single Copies, 15 Cts.

SCIENCE is the official organ of the American Association for the Advancement of Science. Information regarding membership in the Association may be secured from the office of the permanent secretary in the Smithsonian Institution Building, Washington, D. C.

CONSIDERATIONS CONCERNING THE FUNDAMENTALS OF THEORETICAL PHYSICS¹

By Dr. ALBERT EINSTEIN

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SCIENCE is the attempt to make the chaotic diversity of our sense-experience correspond to a logically uniform system of thought. In this system single experiences must be correlated with the theoretic structure in such a way that the resulting coordination is unique and convincing.

The sense-experiences are the given subject-matter. But the theory that shall interpret them is man-made. It is the result of an extremely laborious process of adaptation: hypothetical, never completely final, always subject to question and doubt.

The scientific way of forming concepts differs from

that which we use in our daily life, not basically, but merely in the more precise definition of concepts and conclusions; more painstaking and systematic choice of experimental material; and greater logical economy. By this last we mean the effort to reduce all concepts and correlations to as few as possible logically independent basic concepts and axioms.

What we call physics comprises that group of natural sciences which base their concepts on measurements; and whose concepts and propositions lend themselves to mathematical formulation. Its realm is accordingly defined as that part of the sum total of our knowledge which is capable of being expressed in mathematical terms. With the progress of science, the

¹ Address before the Eighth American Scientific Congress, Washington, D. C., May 15, 1940.

realm of physics has so expanded that it seems to be limited only by the limitations of the method itself.

The larger part of physical research is devoted to the development of the various branches of physics, in each of which the object is the theoretical understanding of more or less restricted fields of experience, and in each of which the laws and concepts remain as closely as possible related to experience. It is this department of science, with its ever-growing specialization, which has revolutionized practical life in the last centuries, and given birth to the possibility that man may at last be freed from the burden of physical toil.

On the other hand, from the very beginning there has always been present the attempt to find a unifying theoretical basis for all these single sciences, consisting of a minimum of concepts and fundamental relationships, from which all the concepts and relationships of the single disciplines might be derived by logical process. This is what we mean by the search for a foundation of the whole of physics. The confident belief that this ultimate goal may be reached is the chief source of the passionate devotion which has always animated the researcher. It is in this sense that the following observations are devoted to the foundations of physics.

From what has been said it is clear that the word foundations in this connection does not mean something analogous in all respects to the foundations of a building. Logically considered, of course, the various single laws of physics rest upon this foundation. But whereas a building may be seriously damaged by a heavy storm or spring flood, yet its foundations remain intact, in science the logical foundation is always in greater peril from new experiences or new knowledge than are the branch disciplines with their closer experimental contacts. In the connection of the foundation with all the single parts lies its great significance, but likewise its greatest danger in face of any new factor. When we realize this, we are led to wonder why the so-called revolutionary epochs of the science of physics have not more often and more completely changed its foundation than has actually been the case.

The first attempt to lay a uniform theoretical foundation was the work of Newton. In his system everything is reduced to the following concepts: (1) Mass points with invariable mass; (2) action at a distance between any pair of mass points; (3) law of motion for the mass point. There was not, strictly speaking, any all-embracing foundation, because an explicit law was formulated only for the actions-at-a-distance of gravitation; while for other actions-at-a-distance nothing was established *a priori* except the law of equality of *actio* and *reactio*. Moreover, Newton himself fully realized that time and space were essential elements, as

physically effective factors, of his system, if only by implication.

This Newtonian basis proved eminently fruitful and was regarded as final up to the end of the nineteenth century. It not only gave results for the movements of the heavenly bodies, down to the most minute details, but also furnished a theory of the mechanics of discrete and continuous masses, a simple explanation of the principle of the conservation of energy and a complete and brilliant theory of heat. The explanation of the facts of electrodynamics within the Newtonian system was more forced; least convincing of all from the very beginning, was the theory of light.

It is not surprising that Newton would not listen to a wave theory of light; for such a theory was most unsuited to his theoretical foundation. The assumption that space was filled with a medium consisting of material points that propagated light waves without exhibiting any other mechanical properties must have seemed to him quite artificial. The strongest empirical arguments for the wave nature of light, fixed speeds of propagation, interference, diffraction, polarization, were either unknown or else not known in any well-ordered synthesis. He was justified in sticking to his corpuscular theory of light.

During the nineteenth century the dispute was settled in favor of the wave theory. Yet no serious doubt of the mechanical foundation of physics arose in the first place because nobody knew where to find a foundation of another sort. Only slowly, under the irresistible pressure of facts, there developed a new foundation of physics, field-physics.

From Newton's time on, the theory of action-at-a-distance was constantly found artificial. Efforts were not lacking to explain gravitation by a kinetic theory, that is, on the basis of collision forces of hypothetical mass particles. But the attempts were superficial and bore no fruit. The strange part played by space (or the inertial system) within the mechanical foundation was also clearly recognized, and criticized with especial clarity by Ernst Mach.

The great change was brought about by Faraday, Maxwell and Hertz—as a matter of fact half-unconsciously and against their will. All three of them, throughout their lives, considered themselves adherents of the mechanical theory. Hertz had found the simplest form of the equations of the electromagnetic field, and declared that any theory leading to these equations was Maxwellian theory. Yet toward the end of his short life he wrote a paper in which he presented as the foundation of physics a mechanical theory freed from the force-concept.

For us, who took in Faraday's ideas so to speak with our mother's milk, it is hard to appreciate their greatness and audacity. Faraday must have grasped

with unerring instinct the artificial nature of all attempts to refer electromagnetic phenomena to actions-at-a-distance between electric particles reacting on each other. How was each single iron filing among a lot scattered on a piece of paper to know of the single electric particles running round in a nearby conductor? All these electric particles together seemed to create in the surrounding space a condition which in turn produced a certain order in the filings. These spatial states, to-day called fields, if their geometrical structure and interdependent action were once rightly grasped, would, he was convinced, furnish the clue to the mysterious electromagnetic interactions. He conceived these fields as states of mechanical stress in a space-filling medium, similar to the states of stress in an elastically distended body. For at that time this was the only way one could conceive of states that were apparently continuously distributed in space. The peculiar type of mechanical interpretation of these fields remained in the background—a sort of placation of the scientific conscience in view of the mechanical tradition of Faraday's time. With the help of these new field concepts Faraday succeeded in forming a qualitative concept of the whole complex of electromagnetic effects discovered by him and his predecessors. The precise formulation of the time-space laws of those fields was the work of Maxwell. Imagine his feelings when the differential equations he had formulated proved to him that electromagnetic fields spread in the form of polarized waves and with the speed of light! To few men in the world has such an experience been vouchsafed. At that thrilling moment he surely never guessed that the riddling nature of light, apparently so completely solved, would continue to baffle succeeding generations. Meantime, it took physicists some decades to grasp the full significance of Maxwell's discovery, so bold was the leap that his genius forced upon the conceptions of his fellow-workers. Only after Hertz had demonstrated experimentally the existence of Maxwell's electromagnetic waves, did resistance to the new theory break down.

But if the electromagnetic field could exist as a wave independent of the material source, then the electrostatic interaction could no longer be explained as action-at-a-distance. And what was true for electrical action could not be denied for gravitation. Everywhere Newton's actions-at-a-distance gave way to fields spreading with finite velocity.

Of Newton's foundation there now remained only the material mass points subject to the law of motion. But J. J. Thomson pointed out that an electrically charged body in motion must, according to Maxwell's theory, possess a magnetic field whose energy acted precisely as does an increase of kinetic energy to the body. If, then, a part of kinetic energy consists of field energy, might that not then be true of the whole

of the kinetic energy? Perhaps the basic property of matter, its inertia, could be explained within the field theory? The question led to the problem of an interpretation of matter in terms of field theory, the solution of which would furnish an explanation of the atomic structure of matter. It was soon realized that Maxwell's theory could not accomplish such a program. Since then many scientists have zealously sought to complete the field theory by some generalization that should comprise a theory of matter; but so far such efforts have not been crowned with success. In order to construct a theory, it is not enough to have a clear conception of the goal. One must also have a formal point of view which will sufficiently restrict the unlimited variety of possibilities. So far this has not been found; accordingly the field theory has not succeeded in furnishing a foundation for the whole of physics.

For several decades most physicists clung to the conviction that a mechanical substructure would be found for Maxwell's theory. But the unsatisfactory results of their efforts led to gradual acceptance of the new field concepts as irreducible fundamentals—in other words, physicists resigned themselves to giving up the idea of a mechanical foundation.

Thus physicists held to a field-theory program. But it could not be called a foundation, since nobody could tell whether a consistent field theory could ever explain on the one hand gravitation, on the other hand the elementary components of matter. In this state of affairs it was necessary to think of material particles as mass points subject to Newton's laws of motion. This was the procedure of Lorentz in creating his electron theory and the theory of the electromagnetic phenomena of moving bodies.

Such was the point at which fundamental conceptions had arrived at the turn of the century. Immense progress was made in the theoretical penetration and understanding of whole groups of new phenomena; but the establishment of a unified foundation for physics seemed remote indeed. And this state of things has even been aggravated by subsequent developments. The development during the present century is characterized by two theoretical systems essentially independent of each other: the theory of relativity and the quantum theory. The two systems do not directly contradict each other; but they seem little adapted to fusion into one unified theory. We must briefly discuss the basic idea of these two systems.

The theory of relativity arose out of efforts to improve, with reference to logical economy, the foundation of physics as it existed at the turn of the century. The so-called special or restricted relativity theory is based on the fact that Maxwell's equations (and thus the law of propagation of light in empty space) are converted into equations of the same form, when they

undergo Lorentz transformation. This formal property of the Maxwell equations is supplemented by our fairly secure empirical knowledge that the laws of physics are the same with respect to all inertial systems. This leads to the result that the Lorentz transformation—applied to space and time coordinates—must govern the transition from one inertial system to any other. The content of the restricted relativity theory can accordingly be summarized in one sentence: all natural laws must be so conditioned that they are covariant with respect to Lorentz transformations. From this it follows that the simultaneity of two distant events is not an invariant concept and that the dimensions of rigid bodies and the speed of clocks depend upon their state of motion. A further consequence was a modification of Newton's law of motion in cases where the speed of a given body was not small compared with the speed of light. There followed also the principle of the equivalence of mass and energy, with the laws of conservation of mass and energy becoming one and the same. Once it was shown that simultaneity was relative and depended on the frame of reference, every possibility of retaining actions-at-a-distance within the foundation of physics disappeared, since that concept presupposed the absolute character of simultaneity (it must be possible to state the location of the two interacting mass points "at the same time").

The general theory of relativity owes its origin to the attempt to explain a fact known since Galileo's and Newton's time but hitherto eluding all theoretical interpretation: the inertia and the weight of a body, in themselves two entirely distinct things, are measured by one and the same constant, the mass. From this correspondence follows that it is impossible to discover by experiment whether a given system of coordinates is accelerated, or whether its motion is straight and uniform and the observed effects are due to a gravitational field (this is the equivalence principle of the general relativity theory). It shatters the concepts of the inertial system, as soon as gravitation enters in. It may be remarked here that the inertial system is a weak point of the Galilean-Newtonian mechanics. For there is presupposed a mysterious property of physical space, conditioning the kind of coordination-systems for which the law of inertia and the Newtonian law of motion hold good.

These difficulties can be avoided by the following postulate: natural laws are to be formulated in such a way that their form is identical for coordinate systems of any kind of states of motion. To accomplish this is the task of the general theory of relativity. On the other hand, we deduce from the restricted theory the existence of a Riemannian metric within the time-space continuum, which, according to the equivalence principle, describes both the gravitational field and the

metric properties of space. Assuming that the field equations of gravitation are of the second differential order, the field law is clearly determined.

Aside from this result, the theory frees field physics from the disability it suffered from, in common with the Newtonian mechanics, of ascribing to space those independent physical properties which heretofore had been concealed by the use of an inertial system. But it can not be claimed that those parts of the general relativity theory which can to-day be regarded as final have furnished physics with a complete and satisfactory foundation. In the first place, the total field appears in it to be composed of two logically unconnected parts, the gravitational and the electromagnetic. And in the second place, this theory, like the earlier field theories, has not up till now supplied an explanation of the atomistic structure of matter. This failure has probably some connection with the fact that so far it has contributed nothing to the understanding of quantum phenomena. To take in these phenomena, physicists have been driven to the adoption of entirely new methods, the basic characteristics of which we shall now discuss.

In the year nineteen hundred, in the course of a purely theoretic investigation, Max Planck made a very remarkable discovery: the law of radiation of bodies as a function of temperature could not be derived solely from the laws of Maxwellian electrodynamics. To arrive at results consistent with the relevant experiments, radiation of a given frequency had to be treated as though it consisted of energy atoms of the individual energy $h\nu$, where h is Planck's universal constant. During the years following it was shown that light was everywhere produced and absorbed in such energy quanta. In particular Niels Bohr was able largely to understand the structure of the atom, on the assumption that atoms can have only discrete energy values, and that the discontinuous transitions between them are connected with the emission or absorption of such an energy quantum. This threw some light on the fact that in their gaseous state elements and their compounds radiate and absorb only light of certain sharply defined frequencies. All this was quite inexplicable within the frame of the hitherto existing theories. It was clear that at least in the field of atomistic phenomena the character of everything that happens is determined by discrete states and by apparently discontinuous transitions between them, Planck's constant h playing a decisive role.

The next step was taken by De Broglie. He asked himself how the discrete states could be understood by the aid of the current concepts, and hit on a parallel with stationary waves, as for instance in the case of the proper frequencies of organ pipes and strings in acoustics. True, wave actions of the kind here required were unknown; but they could be constructed,

and their mathematical laws formulated, employing Planck's constant h . De Broglie conceived an electron revolving about the atomic nucleus as being connected with such a hypothetical wave train, and made intelligible to some extent the discrete character of Bohr's "permitted" paths by the stationary character of the corresponding waves.

Now in mechanics the motion of material points is determined by the forces or fields of force acting upon them. Hence it was to be expected that those fields of force would also influence De Broglie's wave fields in an analogous way. Erwin Schroedinger showed how this influence was to be taken into account, re-interpreting by an ingenious method certain formulations of classical mechanics. He even succeeded in expanding the wave mechanical theory to a point where without the introduction of any additional hypotheses, it became applicable to any mechanical system consisting of an arbitrary number of mass points, that is to say possessing an arbitrary number of degrees of freedom. This was possible because a mechanical system consisting of n mass points is mathematically equivalent to a considerable degree, to one single mass point moving in a space of $3n$ dimensions.

On the basis of this theory there was obtained a surprisingly good representation of an immense variety of facts which otherwise appeared entirely incomprehensible. But on one point, curiously enough, there was failure: it proved impossible to associate with these Schroedinger waves definite motions of the mass points—and that, after all, had been the original purpose of the whole construction.

The difficulty appeared insurmountable, until it was overcome by Born in a way as simple as it was unexpected. The De Broglie-Schroedinger wave fields were not to be interpreted as a mathematical description of how an event actually takes place in time and space, though, of course, they have reference to such an event. Rather they are a mathematical description of what we can actually know about the system. They serve only to make statistical statements and predictions of the results of all measurements which we can carry out upon the system.

Let me illustrate these general features of quantum mechanics by means of a simple example: we shall consider a mass point kept inside a restricted region G by forces of finite strength. If the kinetic energy of the mass point is below a certain limit, then the mass point, according to classical mechanics, can never leave the region G . But according to quantum mechanics, the mass point, after a period not immediately predictable, is able to leave the region G , in an unpredictable direction, and escape into surrounding space. This case, according to Gamow, is a simplified model of radioactive disintegration.

The quantum theoretical treatment of this case is as follows: at the time t_0 we have a Schroedinger wave system entirely inside G . But from the time t_0 onwards, the waves leave the interior of G in all directions, in such a way that the amplitude of the outgoing wave is small compared to the initial amplitude of the wave system inside G . The further these outside waves spread, the more the amplitude of the waves inside G diminishes, and correspondingly the intensity of the later waves issuing from G . Only after infinite time has passed is the wave supply inside G exhausted, while the outside wave has spread over an ever-increasing space.

But what has this wave process to do with the first object of our interest, the particle originally enclosed in G ? To answer this question, we must imagine some arrangement which will permit us to carry out measurements on the particle. For instance, let us imagine somewhere in the surrounding space a screen so made that the particle sticks to it on coming into contact with it. Then from the intensity of the waves hitting the screen at some point, we draw conclusions as to the probability of the particle hitting the screen there at that time. As soon as the particle has hit any particular point of the screen, the whole wave field loses all its physical meaning; its only purpose was to make probability predictions as to the place and time of the particle hitting the screen (or, for instance, its momentum at the time when it hits the screen).

All other cases are analogous. The aim of the theory is to determine the probability of the results of measurement upon a system at a given time. On the other hand, it makes no attempt to give a mathematical representation of what is actually present or goes on in space and time. On this point the quantum theory of to-day differs fundamentally from all previous theories of physics, mechanistic as well as field theories. Instead of a model description of actual space-time events, it gives the probability distributions for possible measurements as functions of time.

It must be admitted that the new theoretical conception owes its origin not to any flight of fancy but to the compelling force of the facts of experience. All attempts to represent the particle and wave features displayed in the phenomena of light and matter, by direct course to a space-time model, have so far ended in failure. And Heisenberg has convincingly shown, from an empirical point of view, any decision as to a rigorously deterministic structure of nature is definitely ruled out, because of the atomistic structure of our experimental apparatus. Thus it is probably out of the question that any future knowledge can compel physics again to relinquish our present statistical theoretical foundation in favor of a deterministic one

which would deal directly with physical reality. Logically the problem seems to offer two possibilities, between which we are in principle given a choice. In the end the choice will be made according to which kind of description yields the formulation of the simplest foundation, logically speaking. At the present, we are quite without any deterministic theory directly describing the events themselves and in consonance with the facts.

For the time being, we have to admit that we do not possess any general theoretical basis for physics, which can be regarded as its logical foundation. The field theory, so far, has failed in the molecular sphere. It is agreed on all hands that the only principle which

could serve as the basis of quantum theory would be one that constituted a translation of the field theory into the scheme of quantum statistics. Whether this will actually come about in a satisfactory manner, nobody can venture to say.

Some physicists, among them myself, can not believe that we must abandon, actually and forever, the idea of direct representation of physical reality in space and time; or that we must accept the view that events in nature are analogous to a game of chance. It is open to every man to choose the direction of his striving; and also every man may draw comfort from Lessing's fine saying, that the search for truth is more precious than its possession.

A COMPLEX VACCINE EFFECTIVE AGAINST DIFFERENT STRAINS OF INFLUENZA VIRUS

By Dr. FRANK L. HORSFALL, Jr., and Dr. EDWIN H. LENNETTE

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IN November, 1939, during the course of certain experiments, four normal ferrets were inoculated intranasally with a strain of epidemic influenza virus obtained during a 1939 epidemic¹. These ferrets developed typical symptoms of experimental influenza, but during convalescence, unexpectedly they began to manifest evidences of a distemper-like infection, and subsequently one died. On the eleventh day after the original inoculation the remaining 3 sick animals were killed. To prevent the spread of the epizootic in the normal ferret colony, a vaccine was prepared from a suspension of the lungs and spleens of these ferrets and was inactivated by the addition of 1:1000 formaldehyde and stored at 4° C. Similar vaccines had been found effective in preventing the spread of ferret distemper on previous occasions.

After inactivation in the icebox for 6 to 10 days, 2 cc of this vaccine was injected subcutaneously into each of 157 normal ferrets. Two days after the vaccination, groups of these animals were inoculated intranasally with the PR8, W.S., or 399 strains of influenza virus. To our great surprise, none of the inoculated ferrets developed experimental influenza. Serum obtained 4 days after vaccination from ferrets which had not been inoculated with influenza virus neutralized both the PR8 and W.S. strains in high dilutions. Serum taken from a number of ferrets prior to vaccination possessed no neutralizing antibodies. These very unexpected findings suggested that the injection of the so-called distemper vaccine had resulted in an inadvertent immunization of almost all the normal ferrets in the laboratory against influenza virus.

¹ F. L. Horsfall, Jr., R. G. Hahn and E. R. Rickard, *Jour. Clin. Invest.*, 19: 379, 1940.

Since this vaccine had been inactivated with formaldehyde and because it appeared to have produced a much broader immunity than resulted from an actual infection with the influenza virus,² it seemed of importance to study this phenomenon more thoroughly. One group of vaccinated ferrets was held for repeated bleedings in order to determine the persistence of antibodies after vaccination. Another group was held for active immunity tests at different intervals following vaccination.

At various intervals during the first 3 months after vaccination sera were obtained from the first group consisting of 15 animals. The neutralizing capacities of the sera from each ferret were determined, and the results are shown graphically in Fig. 1. For purposes of comparison, the results of similar tests on multiple sera from a group of 16 ferrets convalescent from experimental influenza are also shown. The sera from both groups of ferrets were tested against the PR8 strain, since an indication of the extent and the duration of heterologous strain immunity was desired. Line I connects the mean neutralizing capacities of sera obtained from the 15 ferrets at various intervals after vaccination. Line II connects similar values for sera obtained from certain of 16 ferrets at various periods during convalescence from experimental influenza. It will be noted that the serum of vaccinated ferrets possessed almost as much antibody as that of the convalescent animals during the first month. During the second and third months the antibody titers of the convalescent ferrets' sera decreased rapidly, whereas the titers of the sera from the vaccinated ferrets re-

² F. L. Horsfall, Jr. and E. H. Lennette, *Jour. Bact.*, 39: 56, 1940.

remained almost constant. At the end of the third month sera of the vaccinated ferrets were capable of neutralizing 40 times more virus than were the sera of the convalescent animals.

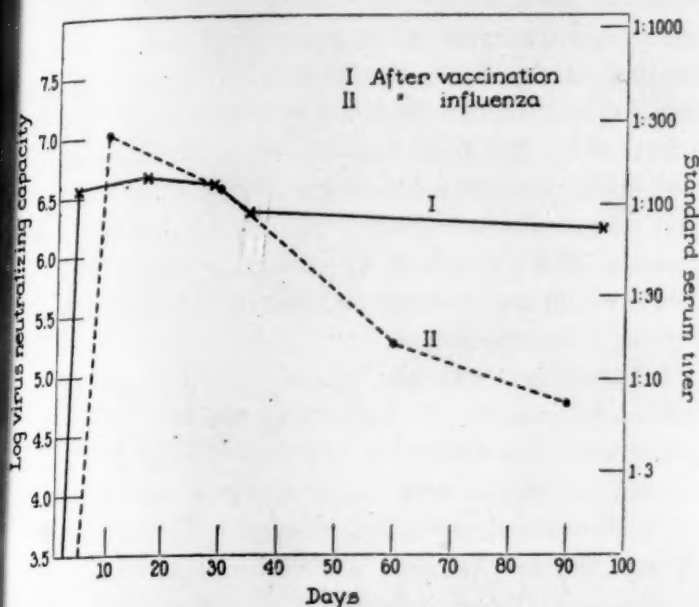


FIG. 1. Mean neutralizing capacities against the PR8 strain of influenza virus of ferret sera taken at various intervals. Line I = sera from 15 ferrets after vaccination. Line II = sera from 16 ferrets after experimental influenza.

The active immunity of vaccinated ferrets was tested by the intranasal inoculation of approximately 1000 infectious doses of the PR8, W.S., or 399 strains of influenza virus. In ferrets these strains had been found to be sufficiently different from each other antigenically to fail to produce reciprocal cross immunity.³ Groups of vaccinated ferrets were tested for the presence of active immunity, 2, 5, 12, 20, 30, and 97 days after vaccination. In most instances serum was obtained before the immunity test and in all cases 10 days afterwards for the determination of neutralizing capacity. The results are summarized in Table I. Ferrets were

TABLE I
IMMUNITY IN VACCINATED FERRETS TO INFLUENZA VIRUS

Number of ferrets in test group	Strain of virus used for immunity test*	Results			
		C. P.	N. C.	Solidly immune	
		Num-ber	Num-ber	Num-ber	Per cent.
14	PR8	0	0	14	100
14	W.S.	1	3	11	78
9	399	0	1	8	89

* 1000 infectious doses given to each ferret.
C.P. Clinical and pathological signs of influenza.
N.C. Increase in virus-neutralizing capacity of serum.

considered to be immune when they failed to manifest typical clinical and pathological signs of ferret influenza and when there was no significant increase in the virus-neutralizing capacity of their sera following inoculation. It will be seen that of 14 ferrets tested

³ *Ibid.*

for immunity against the PR8 strain at various intervals after vaccination, all were immune; of an equal number of vaccinated ferrets tested for immunity against the W.S. strain, 11 were immune; and of 9 ferrets tested for immunity against the 399 strain, 8 were immune. Thus of a total of 37 vaccinated ferrets tested for the presence of active immunity to infection by one or another of three different strains of influenza virus, 33 were solidly immune.

Although this vaccine was found to be surprisingly effective in producing immunity to influenza virus when used relatively soon after preparation, after storage in the icebox for two months it had become entirely ineffective.

Since the symptoms of the secondary infection in the ferrets from which the vaccine was prepared suggested distemper, the vaccinated ferrets were also inoculated with canine distemper virus obtained from the spleen of an infected dog and were found to be immune. This demonstrated that the ferrets from which the vaccine was originally prepared had suffered from a mixed infection of influenza and canine distemper viruses.

The fundamental elements entering into the vaccine were thus established, and the next step in the study was to determine the immunizing efficacy of each of the two virus components alone, following the procedures employed in the preparation of the first vaccine as closely as possible.

Although it was known that during early convalescence from influenza active virus could not be recovered from consolidated ferret lungs, vaccines, both formalinized and non-inactivated, were prepared from the lungs and the spleens of ferrets which had been infected from 8 to 11 days previously with influenza virus. The subcutaneous injection of these vaccines into normal ferrets resulted in neither the production of neutralizing antibodies nor the development of immunity against influenza virus. It therefore seemed unlikely that the effectiveness of the original vaccine could be attributed to influenza virus alone.

Formalinized vaccines were also prepared from the lungs and the spleens of ferrets which had been infected with canine distemper virus alone 12 days previously. Normal ferrets which were given these vaccines subcutaneously did not produce neutralizing antibodies against, or become immune to, influenza virus, although they proved to be immune to dog distemper.

Finally, formalinized vaccines were made from suspensions of the tissues from two ferrets mixed *in vitro*. One of these animals had been infected with influenza virus, while the other had been infected with distemper virus. These vaccines also failed to stimulate either the development of neutralizing antibodies or active immunity to influenza virus in normal ferrets.

These experiments indicated that neither of these two viruses alone was capable of producing effective vaccines and that *in vitro* mixtures of the two were ineffective. The evidence suggested, therefore, that, in order to have effective vaccines, it was essential for both viruses to produce infections in the same host concurrently.

In order to ascertain whether a vaccine possessing an immunizing efficacy equal to that of the original preparation could be reproduced at will, ferrets were inoculated with mixtures of both influenza and distemper viruses and were killed at various intervals thereafter. Formalinized vaccines were prepared from their lungs and spleens, repeating the original procedure. These vaccines were tested in normal ferrets, and at various intervals thereafter the serum of the vaccinated animals was tested for the presence of neutralizing antibodies. The animals themselves were also tested for active immunity to influenza virus.

It soon became apparent that it was not easy to prepare vaccines as effective as the original preparation. A large number of different vaccines were prepared from the tissues of ferrets which had been infected with both viruses. The duration and the severity of the two infections were varied. Separate tissues or mixtures of tissues were used in preparing the vaccines, and the procedure of inactivation was altered in a number of ways. Most of these preparations proved

to be entirely ineffective. It has been possible, however, to prepare vaccines capable of producing active immunity in ferrets against influenza virus. Ferrets which were given these vaccines and subsequently inoculated intranasally with 1,000 infectious doses of heterologous strains of influenza virus showed neither the typical signs of infection nor an increase in neutralizing antibodies, indicating conclusively that no infection by the virus had occurred. Because of the number of variables which are related to the production of an effective vaccine of this kind, much more study will be required to determine the conditions under which an effective immunizing preparation can regularly be reproduced.

This vaccine was also tested on small groups of human volunteers. It was found that a vaccine prepared from the tissues of ferrets suffering from concurrent infections with influenza virus and the strain of distemper virus isolated from spontaneously infected ferrets produced a definite increase in antibodies neutralizing influenza virus in every instance. Another lot of vaccine prepared identically, but using a strain of distemper virus recently isolated from the spleen of an infected dog, failed to stimulate influenza antibody production in human volunteers. Experiments are in progress to determine the duration of the demonstrable immunity in man produced by the complex vaccine.

OBITUARY

MAYNARD MAYO METCALF

MAYNARD MAYO METCALF died on April 19, 1940, at "The Rambles," on Alabama Drive, Winter Park, Florida, where he and Mrs. Metcalf had spent the last two entire years, and the preceding two winters.

Ever since leaving the Johns Hopkins University in 1893, with the doctorate from Professor W. K. Brooks, the *pater noster* of so many distinguished American zoologists, Dr. Metcalf was so prominent a figure, as officer or contributor of papers, at meetings of learned societies, that many readers of this memorial will feel that they already know the man thoroughly well. His cordiality, rare friendliness and quick understanding made him the center of congenial groups, not only of biologists but of economists, sociologists, political scientists and Christian ministers—so broad and active was his interest in all these and other fields.

Of English ancestry fully on record from 1360 to the present, he was born in Elyria, Ohio, on March 12, 1868, of Eliab Wight Metcalf and Eliza (Ely) Metcalf. He was of a family more continuously and significantly represented at Oberlin College than any other, himself receiving the B.A. in 1889 and the honorary Sc.D. in 1914.

On completing graduate study at Johns Hopkins University he relinquished a post-doctorate Bruce fellowship to accept appointment as organizer and chairman of the department of biology at "The Woman's College" (now Goucher), where he remained until 1906, his choice of successor being the late William E. Kellicott—an item which he referred to later as his "best service to the institution." Although his appointment as chairman and reorganizer of the department of zoology at Oberlin began in 1906, laboratory space was not then in readiness; and the next two years were spent in research with Boveri in Wurzburg, in Berlin and at the Naples Biological Station.

He resigned official relation with Oberlin in 1914; but during the preceding eight years gave time, energy and wisdom unsparingly to the development of the department, himself supplying much equipment the college was not in position to afford. His inspiration and ideals have been the major factor in shaping such progress as the Oberlin department has made from his day to the present. Research in his private "Orchard Laboratory," at La Jolla, Calif., Washington, D. C., Baltimore and in South America occupied the years 1914 to 1924. Then for a year he was chairman of

the division of biology and agriculture of the National Research Council. From 1926 to 1933 he was research associate, with professorial rank in zoology, at the Johns Hopkins University. Thereafter, impaired health compelled retirement, with only occasional scientific effort. Many summers from 1890 until 1935 were spent at Woods Hole, at the U. S. Fisheries Station or at the Marine Biological Laboratory, of which he was trustee 1896 to 1932, and emeritus thereafter.

Metcalf's publications include more than 125 titles, besides two books and other extended treatises. His earlier research studies were concerned with gastropods and tunicates (24 papers); his later interest centered in the protozoa, with special emphasis on the Opalinids, on which a major comprehensive work is now being issued by the U. S. National Museum. His membership in national and philanthropic societies included twenty-eight American, three British and three French. His official responsibilities in several of these are listed in "Who's Who." He was a member of the Authors Club, London.

He is survived by his wife, Ella Wilder Metcalf, of the same college class; a daughter, Mrs. William P. Beetham, and three grandchildren, of Waban, Mass.; and by a brother, Dr. Wilmot V. Metcalf, formerly professor of physical sciences in Carleton College and Fisk University, now residing in Clinton, N. Y.

Few men indeed meet life with the degree of fascination with things serious, *e.g.*, science, politics, philoso-

phy, religion; in enjoyment of beauty—either in nature or of human production; in good fun and sport (an ardent golfer), as did Maynard Metcalf. He was a man of severely discriminating judgment, of positive opinions, of uncompromising devotion to integrity; he called himself "frankly Christian," a fact which we may allow showed itself in his spontaneous sympathies, his chronic cheerfulness and in the generosity of his spirit.

ROBERT A. BUDINGTON

OBERLIN COLLEGE

RECENT DEATHS

DR. ALVIN SAWYER WHEELER, Kenan professor emeritus of organic chemistry at the University of North Carolina, died on May 12 in his seventy-fourth year.

LEWIS VAN CARPENTER, professor of sanitary engineering at the College of Engineering of New York University and director of the Sanitary Engineering Research Laboratory conducted jointly by the college and the city, died on May 10 in his forty-fifth year.

DR. HUNTER ROBB, professor of gynecology of the School of Medicine of Western Reserve University, died on May 15 at the age of seventy-seven years.

DR. CHARLES DAVISON, an authority on earthquakes, died in Cambridge, England, on April 29 at the age of eighty-one years.

SCIENTIFIC EVENTS

THE ANNUAL REPORT OF THE FIELD MUSEUM OF NATURAL HISTORY

THE annual report for 1939 of the Field Museum of Natural History, of which Dr. Clifford C. Gregg is director, has been issued. It states that gifts and bequests of funds amounting to more than \$730,000 were received during the year. Dr. Gregg points out that "the steadily decreasing rates of return from investments, and some degree of fear for the future on the part of citizens resulting in fewer contributions, combine to make the financial administration of this museum and other institutions similarly supported an increasingly difficult problem. A recent decision of the Illinois Supreme Court made inoperative the so-called 'museums act,' which brought to this institution approximately \$100,000 per year from taxes as a contribution toward its maintenance."

The report presents a detailed outline of the activities of the museum administration, the scientific departments, the educational departments and the various small divisions entrusted with special phases of museum activities.

Dr. Gregg states:

1,410,454 people visited the museum in 1939. Of these, 94.1 per cent. were admitted free, and only 5.9 per cent. paid the twenty-five cent admission fee charged on certain days of the week. More than 100,000 persons attended free lectures for adults and free motion picture programs for children in the James Simpson Theatre of the museum, and lecture tours and other special events. Contact was made with 186,677 children in their schools through lectures presented in classrooms and assemblies by members of the staff of a museum division known as the James Nelson and Anna Louise Raymond Foundation for Public School and Children's Lectures. Approximately 500,000 children were served by the natural history lessons presented in traveling exhibits circulated on a bi-weekly schedule in all of Chicago's public schools, and many parochial, private and special schools as well. This activity is carried out through the museum department known as the N. W. Harris Public School Extension.

Combining the total number of visitors to the museum with the total of the children reached outside the institution by the Raymond Foundation and the Harris Extension, it is found that the museum's cultural influence was again extended directly to more than two million persons. In addition, there are the usual further extensions to incalculable numbers reached through less direct media such

as radio programs, publications and leaflets, and articles in newspapers and magazines.

The museum had ten expeditions in operation in the United States and foreign countries during 1939, and considerable field work on a smaller scale was also conducted. This extension of activity became possible only through the generosity of patrons who sponsored the most important expeditions. Without such assistance, the museum would have been unable to allocate adequate funds for this purpose.

The expeditions included one, sponsored by Stanley Field and led by Dr. Wilfred H. Osgood, chief curator of zoology, to collect specimens of the fauna of Peru, Bolivia, Chile and the shores of the Straits of Magellan; the Field Museum Archeological Expedition to the Southwest, also sponsored by Stanley Field, which excavated prehistoric American Indian sites in New Mexico under the direction of Dr. Paul S. Martin, chief curator of anthropology; botanical expeditions to Guatemala, the southwestern United States and Mexico; a zoological expedition to British Guiana; an ornithological expedition to the Yucatan Peninsula; paleontological expeditions to Colorado, South Dakota and Nebraska, and an expedition to collect and study the marine fauna along the Atlantic and Gulf coasts of Florida. A project for the making of photographs of type specimens of plants in the leading herbaria of Europe, conducted steadily since 1929 by J. Francis Macbride, associate curator of the herbarium, was continued through most of 1939.

Twenty-eight technical scientific publications, circulated internationally among museums, libraries, other institutions and individual scientists, were issued by Field Museum Press. The museum became a member of the University Broadcasting Council, to participate in educational work by radio; and, in cooperation with the Zenith Radio Corporation, presented experimental programs by television.

It is stated that the Works Progress Administration has taken an active part in the work of the museum. More than 262,000 hours of work were done by a force of from 125 to 219 persons.

THE STRUCTURAL STEEL WELDING RESEARCH COMMITTEE OF THE ENGINEERING FOUNDATION

THE formation of a Structural Steel Welding Research Committee to study problems of design and fabrication in the building field is announced by the Engineering Foundation.

Leon S. Moisseiff, New York consulting engineer and designer of the George Washington and Triboro bridges in New York and the Golden Gate and San Francisco-Oakland Bay bridges, has been chosen chairman. Other members are: F. H. Frankland, technical director of the American Institute of Steel Construc-

tion, New York; Jonathan Jones, chief engineer of Fabrication Division, Bethlehem Steel Corporation, Bethlehem, Pa.; C. H. Goodrich, chief engineer of the American Bridge Company, Pittsburgh, Pa.; A. S. Low, vice-president of the Austin Company, Cleveland, Ohio; Commander C. A. Trexel, design manager, Bureau of Yards and Docks, United States Navy, Washington, D. C.; La Motte Grover, engineer, Air Reduction Sales Company, New York; Professor Bruce Johnston, of Lehigh University. H. W. Lawson, engineer, Bethlehem Steel Corporation, and F. H. Dill, engineer, American Bridge Company, have been named alternates.

The program includes the establishment of research fellowships in American universities. The first fellowship goes to Lehigh University for a two-year period and carries with it an annual stipend of \$1,100. Other fellowships will be established as soon as the committee maps a complete program of research projects. The investigations at Lehigh will be directed toward developing a satisfactory design procedure for beam-to-girder and beam-to-column connections for all kinds of welded building construction. The official statement points out:

The work of the committee, in general, will be to secure basic data which will enable fabricators to apply welding in building with greater safety and with greater economy. By obtaining full information on the effects of varying loads on all classifications of welded connections, the committee hopes to perform a service for building engineers and aid them in setting up different formulas which will be applicable in each type of construction. At present there is a wide diversity of opinion regarding the best designs for various welded connections.

It is important that engineers have at least one continuing body from which the results of research in this field can be obtained. Formation of the committee will also assist the engineering profession in seeing to it that the development of structural welding is scientific and sound.

The Committee was organized by the Welding Research Committee of the Engineering Foundation, working in cooperation with the American Institute of Steel Construction. It is proposed that the research work of the new group should tie in with the studies in welding literature, the fundamental research investigations now underway in various universities, and the projects of the Industrial Research Division, all of which are sponsored by the Welding Research Committee.

The first Structural Steel Research Committee was established about fifteen years ago, but was discharged in 1938 after having exhausted its funds and completed the work originally outlined. The outstanding contribution of the body was the formulation of the Amer-

ican Welding Society Building Code, which now is in standard use in more than 200 municipalities, including New York City, Chicago and Pittsburgh.

THE CHICAGO MEETING OF THE INSTITUTE OF FOOD TECHNOLOGISTS

FINAL plans for the first annual meeting of the Institute of Food Technologists are taking definite form. As announced early in January, the meeting is to be held in the Morrison Hotel, Chicago, from June 17 to 19, inclusive. Registration will begin at 3:00 P.M. on Sunday, June 16.

The technical sessions open at 9:30 A.M. on Monday, with a discussion of the "Process Engineering in Food Technology." Dr. L. V. Burton, editor of *Food Industries* and chairman of the session, will speak on "Engineering a Food Manufacturing Process"; W. L. Badger, of the Dow Chemical Company, on "Application of the Unit Operations of Chemical Engineering to the Food Industries"; G. T. Reich, of the Pennsylvania Sugar Company, on "Engineering a Continuous Evaporation and Hydrolysis Process," and Dr. N. E. Berry, of the General Foods Corporation, on "The Chemical Engineer Looks at a Food Process."

The Monday afternoon session will be presided over by the president of the institute, Professor Samuel C. Prescott, dean of science of the Massachusetts Institute of Technology, and will be devoted to a program of seven voluntary papers on food technology. Subjects ranging from mechanism of heat transfer, sanitary principles in dairy equipment design and germicidal efficiency of washing solutions for glass containers to moisture content of staple dietary foods, vitamin B₁ potency of malt and brewed beverages and securing food for an army complete the program for the session.

"The Effect of Processing on the Vitamin Content of Foods" will be discussed in a symposium under the chairmanship of Dr. George C. Supplee, of Borden and Company, when Dr. C. A. Elvehjem, of the University of Wisconsin, will discuss "The Nature of Vitamins with Particular Reference to the B Complex." Vitamins A, B₁, C, D and G will be taken up in turn and dealt with in respect to their stability under food-processing conditions.

Contrary to the procedure followed in the first three technical sessions, the Tuesday afternoon program will be presented in four divisions with each division having its own program of six or seven papers with meetings held concurrently. Division A will discuss problems and practices relative to the packaging of foods; Division B will deal with the technology of food preservation with emphasis on the chemical aspect of the subject; Division C, while spending some time on methods of analysis, will focus attention on the control of unit operations in food processing; Division D will

emphasize the microbiology of foods with respect to flavor development and preservation factors.

A smoker is planned for Monday evening. All men registrants at the meeting will be guests of the Chicago group. The annual dinner will be given on Tuesday evening. The last day has been reserved for plant visits in the Chicago area.

EXHIBITION OF THE WORKS OF LEONARDO DA VINCI

THE exhibition of the works of Leonardo da Vinci, held for over a year in the Palace of Arts in Milan, Italy, is being brought to the United States. Eighteen large roomfuls of material pertaining to his life and work, including working models of his inventions and his works of art, were shipped on April 30 on the *Barberigo* from Genoa. The exhibition will first be shown to the American public at New York's Museum of Science and Industry in Radio City and will be opened to the public in the early part of June.

Three years were spent by the Italian Government in assembling the exhibition, many items of which, such as the fourteen volumes of Leonardo's original autograph writings and his studies for works of art lost or unfinished, have for centuries remained in private collections. Hundreds of thousands of dollars have been spent by the Italian Government in building models of one hundred and seventy of Leonardo's scientific inventions, which range from an apparatus for measuring the earth to a heat-operated roasting oven. All these inventions, including his plans for flying machines, his submarine, his differential gear for vehicles and other features of modern life, conceived 400 years ago, will be represented by full-size or scale models made from his own drawings and specifications, which will be exhibited together with the models themselves. The announcement points out:

Most popularly known as the painter of the "Mona Lisa" and the "Last Supper," Leonardo da Vinci was centuries ahead of his age in every department of art and science he put his mind to. In the days when ships were propelled by wind and oars he understood the power of steam. He planned cities of the future with superimposed highways, and designed circular forts with underground passages that are not a far cry from France's Maginot Line or Germany's West Wall. A hundred years before Gutenberg was born he had invented a printing press; his anatomical studies with Antonio della Torre, of Pavia, revolutionized the world of medicine. He was a great biologist, physicist and musician. He even invented a diving apparatus, but refused to disclose his plans to any one because, as he said, man's "wickedness and ferocity" would enable him to walk on the bed of the ocean and do damage to ships and those sailing in them.

One of the features of the New York exhibition, ac-

cording to Robert P. Shaw, director of the museum, will be the actual operation of the Leonardo models. His printing press will be operated as in his own day, and his mint, made at the behest of the Medici, will turn out such coins as were minted for the Florentine

Republic 400 years ago. So many and varied are the inventions that only those that corresponded with his own age were used during his lifetime. The majority remained on paper, awaiting the day when civilization should advance to the point where it could use them.

SCIENTIFIC NOTES AND NEWS

PROFESSOR CASWELL GRAVE, head of the department of zoology at Washington University, St. Louis, having reached the age of seventy years, retired from active work on February 1 and became professor emeritus of zoology. At a dinner given on May 11, widely attended by his colleagues, students and friends, it was stated that a scholarship had been established in his honor, which had been made possible by contributions from his many friends. It will be called the Caswell Grave Scholarship for Biological Research and will be awarded annually to a qualified student at Washington University to defray the cost of tuition and partial expenses of attending course work at the Marine Biological Laboratory, Woods Hole, Mass. At the dinner Professor Grave was also presented with a bound volume of personal letters of greeting. He plans to spend his summers at Woods Hole and his winters at Winter Park, Fla.

At the recent meeting of the trustees of Science Service, Dr. Harlow Shapley, Paine professor of astronomy at Harvard University and director of the Harvard Observatory, was elected vice-president and chairman of the executive committee. He succeeds Dr. William H. Howell, emeritus professor of physiology at the Medical School of the Johns Hopkins University, who wished to retire after serving for ten years. An informal luncheon to welcome Dr. Shapley was given by the staff of Science Service at the Cosmos Club, Washington, on May 15.

AN honorary degree will be conferred on Dr. Thomas Parran, Surgeon General of the U. S. Public Health Service, in connection with the commencement exercises in June of St. Bonaventure College, New York.

DR. STUART LESSLEY CRAIG, an alumnus of the Medical College of Virginia, Richmond, surgeon and a director of the New York Eye and Ear Infirmary, New York City, will be awarded the honorary degree of doctor of science at the graduation exercises of the college.

At the forty-third annual meeting of the American Society for Testing Materials during the week beginning on June 24, the fourteenth award of the Charles B. Dudley Medal will be made to T. F. Willis and M. E. De Reus, research engineer and junior engineer, respectively, of the Bureau of Materials of the Missouri

State Highway Department, Jefferson City, Mo., for their paper on "Thermal Volume Change and Elasticity of Aggregates and Their Effect on Concrete." The fifteenth Edgar Marburg Lecture will be presented by P. H. Bates, chemist of the National Bureau of Standards. He will speak on "Portland Cement—Theories and Specifications."

ROYAL MEDALS of the Royal Geographical Society have been awarded as follows: The *Founder's Medal* to Mr. and Mrs. Harold Ingrams for their exploration, travel and studies in the Hadhramaut and the *Patron's Medal* to Lieutenant Alexander R. Glen, for his expeditions in Spitsbergen and North-East Land. The council has made the following awards: The *Victoria Medal* to O. G. S. Crawford, for his archeological maps prepared for the Ordnance Survey and his work on the *Tabula Imperii Romani*. The *Murchison Grant* to Peter Mott, for his surveys in West Greenland; the *Back Grant* to Gerald Seligman, for his glacier studies on the Jungfrauoch; the *Cuthbert Peek Grant* to John Hanbury-Tracy, for his work in southeastern Tibet with Mr. Kaulback and his journey in the north of South America; the *Gill Memorial* to Alexander King, for his work in Jan Mayen in 1938.

THE Ettore Marchiafava Prize, founded by the University of Rome in October, 1938, for the best work on morbid anatomy or general pathology, has been awarded to Professor Mario Monacelli, director of the Dermatological Clinic of the University of Messina, and Professor Giulio Raffaele, of the University of Rome.

DR. HENRY A. SCHUETTE, professor of chemistry at the University of Wisconsin, was elected president of the American Oil Chemists' Society at the close of the annual meeting in New Orleans on May 10.

DR. SAMUEL FREDERICK HILDEBRAND, senior ichthyologist of the U. S. Bureau of Fisheries, has been elected to resident membership in the Washington Academy of Sciences in recognition of his "demonstration of the utility of fishes in mosquito control, his work on the life histories of marine fishes of the Atlantic coast and his contributions to the ichthyology of Central America."

AFTER forty years of teaching, Professor Cora J. Beckwith, chairman of the department of zoology at Vassar College, will resign in June. Professor Rudolf

T. Kempton has been appointed chairman of the department.

PROFESSOR C. E. MCCLUNG, of the University of Pennsylvania, has been appointed visiting professor of zoology at the University of Illinois for the year 1940-41; Professor Victor E. Shelford has been appointed chairman of the department of zoology.

PROFESSOR WALTER H. BUCHER, head of the department of geology of the University of Cincinnati, has been appointed professor of geology at Columbia University. He will have charge of graduate work in structural geology.

DR. TH. DOBZHANSKY, professor of genetics at the California Institute of Technology, has been appointed professor of zoology at Columbia University. Dr. Marcus M. Rhoades, geneticist of the U. S. Department of Agriculture, has been appointed associate professor of botany. Professor Dobzhansky and Dr. Rhoades will direct research in the laboratory of genetics which was established two years ago to unite work in botany and zoology. They will collaborate with Professor Leslie Dunn, who will become head of the department of zoology on July 1.

W. W. WATSON, associate professor at Yale University, has been promoted to be professor of physics and chairman of the department of physics. Professor Watson succeeds Professor John Zeleny, who retires this year. Dr. George H. Smith, professor of immunology, has been appointed assistant dean of the Yale School of Medicine for the next college year, and Dr. Adolf Magnus-Levy has been appointed research associate in physiology with the rank of professor. Dr. G. Evelyn Hutchinson has been promoted to an associate professorship of zoology.

PROFESSOR HAROLD E. BURTT has been made chairman of the department of psychology at the Ohio State University. He has been serving as acting chairman of the department since the death of Dr. George F. Arps on September 16, 1939.

DR. L. P. ALFORD, professor of administrative engineering and chairman of the department of industrial engineering at New York University, has been made chairman of a newly established department of administrative engineering at Cornell University. In addition to a four-year curriculum leading to the degree of bachelor of administrative engineering, the new department will offer a post-senior course for graduates of engineering schools and certain accredited graduates of liberal arts colleges, which will lead to the baccalaureate degree in the field of administrative engineering.

DRS. O. N. ALLEN, Williard H. Eller and C. J. Hamre, associate professors of bacteriology, physics

and zoology, respectively, have been promoted to the rank of full professor at the University of Hawaii, effective in September.

A GRANT has been made by the Rockefeller Foundation to Duke University for one year in support of the investigation of problems in physical chemistry by Dr. Hans Neurath, assistant professor of biochemistry. A Field Nutrition Study has been established at the university in cooperation with the Rockefeller Foundation and the State Board of Health. Sera coming from a survey area in a rural section are tested in the nutrition laboratory, and medical and dietetic studies will be carried on in the field.

REAR ADMIRAL RICHARD E. BYRD, leader of the U. S. Antarctic Expedition, has arrived in the United States after a five-months absence in Little America. He brought with him a map of the nine hundred mile stretch of hitherto unknown Antarctic coast line, charted at the request of the Navy.

NORMAN NEVILLS will lead an expedition of nine on a trip down the Green and Colorado Rivers, leaving Green River, Wyo., on June 20, and arriving at Boulder Dam about August 25. The group will travel in three specially designed boats and will make botanical and geological observations and collections. Dr. Hugh C. Cutler, of Washington University, is in charge of botanical research, and Mr. Nevills of the geological work.

DR. JAMES E. ACKERT, dean of the Division of Graduate Study and professor of zoology at Kansas State College, Manhattan, delivered the annual out-of-state address before the Medical Science Society of the Oklahoma University School of Medicine on May 8. The subject of the lecture was "Nematode Host-Parasite Relationships."

DR. REGINALD FITZ, lecturer on the history of medicine at the Harvard Medical School, will be the commencement speaker at the Medical College of Virginia, Richmond.

DR. KARL PAUL LINK, professor of biochemistry at the Wisconsin State Agricultural Experiment Station, delivered the annual Phi Lambda Upsilon lecture at the University of Illinois on April 22. He discussed the results of six years of biochemical studies on the genus *Melilotus*.

THE fifth annual Hughlings Jackson lecture of the Montreal Neurological Institute will be given at the institute on October 3 by Dr. Charles H. Best, professor of physiology, University of Toronto. His subject will be "The Factors Affecting the Liberation of Insulin from the Pancreas."

DR. KURT KOFFKA, William Allan Neilson research professor of psychology at Smith College, delivered

during the present month four lectures on human behavior in the Nuffield Institute of the University of Oxford.

THE fifth Pan-American Congress of Tuberculosis will be held from October 13 to 17 in Buenos Aires and Cordoba. Papers to be presented may be submitted until July 1 and titles of contributions to these subjects until September 1.

A SOCIETY of the History of Medicine has recently been founded in Peru. Its aim is to further the progress of medical history, especially that of Peru, and to cultivate relations with foreign countries, especially France. Several French medical historians have been elected honorary members of the new society.

THE annual meeting of the American Psychological Association will be held at the Pennsylvania State College from September 4 to 7. Meeting concurrently with the association will be the Psychometric Society, the Association for Applied Psychology, the Society for the Psychological Study of Social Issues and the American Speech Correction Association.

THE fifty-fourth annual convention of the Association of Land-Grant Colleges and Universities will be held in Chicago on November 11, 12 and 13; pre-convention dates are November 8 to 10, inclusive. Headquarters will be at the Drake Hotel.

THE forty-second annual meeting of the Medical Library Association will be held at the Medical Schools of the University of Oregon, Portland, on June 25, 26 and 27, under the presidency of Colonel Harold W. Jones, of the Army Medical Library, Washington, D. C. Hotel headquarters will be at the Heathman. The program will include talks on the literature of epidemiology of plague, tularemia and Rocky Mountain spotted fever; a symposium on investigations in local medical history, and problems in bibliography based on a study of terminology in the field of nutrition.

THE annual spring meeting of the Indiana Academy of Science was held on May 3 and 4, in Spring Mill State Park. On the first day the program included papers on geology and physiography and the fauna and flora of the region, with field trips on the second day conducted by Professor Louis Agassiz Test, of Purdue University; Professor Clyde A. Malott, of Indiana University; Professor Ray C. Friesner, of Butler University, and O. E. Ackerson, of the State Conservation Department. Frank N. Wallace, state entomologist, is president of the academy.

THE seventh annual meeting of the New York State Geographical Association will be held on October 12 at Rochester, N. Y. There will be papers and reports, a field trip under the leadership of the Monroe County

Planning Board, and a dinner in the evening. Meetings will be held in the Geology Building and Museum of the university. A tentative program can be obtained after September 25 from Robert Simpson, of the department of geology, who is chairman of the meeting.

THE sixth biennial convention of Alpha Epsilon Delta, national honorary pre-medical fraternity, was held with the Oklahoma Alpha chapter at the University of Oklahoma on March 21, 22, 23, 1940, under the presidency of Dr. Charles F. Poe. Following the initiation of candidates by the Oklahoma Alpha chapter, Dr. Felix M. Adams, Eastern Oklahoma State Hospital for the Insane, Vinita, Okla., gave a lecture on "Insulin Shock and Metrazol Treatment," which was illustrated with a film in technicolor. Tours were made of the University of Oklahoma Medical School at Oklahoma City and the Central Oklahoma State Hospital at Norman. On Friday evening, at an Indian dinner and program, members were initiated into the secrets of the training of the Indian medicine man. The convention banquet was held at the Biltmore Hotel, Oklahoma City, on Saturday evening, at which Dr. Henry H. Turner, assistant professor of medicine, School of Medicine, University of Oklahoma, spoke on "The Wagner Health Bill," and Dr. Wendell Long, Oklahoma City, presented "A Brief History of Medicine."

THE Research Council on Problems on Alcohol plans the publication of a quarterly journal on alcohol to be the official organ of the council. It will be published at Yale University. Dr. Howard W. Haggard, associate professor of applied physiology in the Sheffield Scientific School, has been appointed editor. Funds have been made available, through the efforts of Dr. Haggard, to finance the publication for a five-year period. The executive committee has appointed an editorial committee on general policy.

THE first number of a new monthly scientific journal entitled *Ciencia, Revista hispano-americana de Ciencias puras y aplicadas*, published in Mexico City, appeared on March 1. It is edited by a group of scientific men exiled from Spain, headed by Professor Ignacio Bolivar, entomologist and formerly director of the Museum of Natural History of Madrid, with the cooperation of Professors C. Bolivar, I. Costero and F. Giral. In the list of seventy-one collaborators are included scientific men from the American continent and a few from Europe. The North American countries are represented by Drs. Lorente de N6, New York; R. Matas, New Orleans; J. F. Nonidez, New York; Prados, Montreal, and M. S. Vallarta, Cambridge, Mass. The review is published in Spanish. Each number contains seven sections: I. Modern science, giving bibliographical reviews of diverse sci-

tific topics; II. Short original articles; III. News; IV. Applied science; V. Miscellaneous; VI. New books, and VII. Abstracts of scientific articles.

ON behalf of the committee of the Joseph Henry Fund of the National Academy of Sciences the following grants have been made: \$575 to Professor A. Franklin Shull, of the department of zoology, University of Michigan, to be used for the purchase of an automatic calculating machine for his researches on the developmental processes and embryonic determination in aphids, and \$400 to Dr. Dorothy Wrinch, visiting lecturer in the department of chemistry of the Johns Hopkins University, to defray the expenses of computations involved in the interpretation of x-ray data in the study of the structure of certain protein molecules, particularly insulin and lactoglobulin.

SIR JOHN SIMON announced in the House of Commons recently, according to the *London Times*, that Parliament would be invited in the estimates, shortly to be presented, to maintain the provision made for the universities and colleges at the existing level—namely, £2,149,000. He added that the government

was fully conscious of the vital part played by the universities in the national life and of the importance of maintaining the standards of university education as far as possible in the strained conditions of war. He was satisfied that the maintenance of the present financial provision was necessary if the universities were to continue to make their essential contribution in various ways to the present national effort. Local authorities, he hoped, would take similar action.

THE *Australian Journal of Science* announces that by an arrangement between the government and the University of Adelaide, the Adelaide Observatory is to become more closely associated with the university. It is expected that its present site will be made available for the Adelaide Boys' High School. A new building is to be provided for the observatory within the university grounds adjacent to the Physics and Engineering Building. The government astronomer, G. F. Dodwell, will be in charge, and it is expected that cooperation between the observatory and the physics department will allow students in physics to receive some teaching in astronomy.

DISCUSSION

RELEASE OF ACETYLCHOLINE BY SYMPATHETIC GANGLIA AND SYNAPTIC TRANSMISSION

EXPERIMENTS performed by the writer¹ on the release of acetylcholine by the superior cervical sympathetic ganglion and the nodosum ganglion of the vagus nerve have yielded results that differ in important details from those previously reported by Feldberg and Vartiainen.² The problem of the release of acetylcholine by these structures has again been investigated by MacIntosh,³ and in making reference to his work, Sir Henry Dale⁴ has recently remarked that the validity of the fundamental observation made by Feldberg and Vartiainen, although challenged by me, has been effectively reinstated by MacIntosh, whose evidence "must stand until it has been directly answered." The discussion which follows will show that MacIntosh's results do in fact disagree with some of my own findings, but that they also disagree with results previously obtained in the same laboratory by Feldberg and his collaborators.

At the start of the artificial perfusion of the superior cervical ganglion, and in the absence of stimulation and of peripheral response, there may appear significant outputs of A.Ch., which do not prevent the prompt appearance of a peripheral response upon

stimulation of the preganglionic trunk. Initial spontaneous outputs had occasionally been observed by Gaddum and Feldberg⁵ and had been described by Brown and Feldberg⁶ in these words: "The venous effluent at the beginning of the perfusion of a ganglion with an eserinated Locke solution often contains some A.Ch., the concentration being rarely higher than 0.01 γ per cc. The concentration decreases regularly and A.Ch. has usually disappeared after less than 30 min. perfusion." In a subsequent paper Brown and Feldberg⁷ report that after several minutes of stimulation, synaptic transmission with a well maintained peripheral response is accompanied by the release of A.Ch. by the ganglion in the concentration of 0.01 γ per cc. Therefore, the existence of "spontaneous" outputs of A.Ch. in similar concentrations, but without synaptic transmission, must be regarded as significant. In my early experiments, in which the ganglion was prepared for perfusion according to the technique described by Gaddum and Feldberg and Feldberg and Vartiainen, initial spontaneous outputs as described by these investigators were observed, but later, after improvements in the technique of dissection of the ganglion had been introduced,⁸ the initial spontaneous outputs of A.Ch. became very small or even failed to appear. In MacIntosh's experiments the concentration of A.Ch. in the

¹ R. Lorente de N , *Amer. Jour. Physiol.*, 121: 331, 1938.

² W. Feldberg and A. Vartiainen, *Jour. Physiol.*, 83: 103, 1934.

³ F. C. MacIntosh, *Jour. Physiol.*, 94: 155, 1938.

⁴ H. Dale, *SCIENCE*, 90: 393, 1939.

⁵ J. H. Gaddum and W. Feldberg, *Jour. Physiol.*, 81: 305, 1934.

⁶ G. L. Brown and W. Feldberg, *Jour. Physiol.*, 86: 290, 1936.

⁷ *Ibid.*, 88: 265, 1936.

⁸ R. Lorente de N , *op. cit.*, p. 336.

initial spontaneous output, when there was any, was very small.

In some of the experiments made with the improved technique of dissection of the ganglion, preganglionic stimulation resulted in an output of A.Ch. in concentrations several times smaller than those I had observed in perfusions performed by the original technique.^{9,10} In fact, in one instance the output of A.Ch., if any had taken place, was so small that it did not reach the threshold of the leech preparation that was being used. For this and other reasons given in the original paper the conclusion was reached that initial spontaneous output of A.Ch. and its release in amounts larger than those observed at the start of successful perfusions, was a pathological phenomenon. Taking the last experiment as a paradigm, it may be said that the upper limit of the amount of physiologically released A.Ch. could not be more than 4×10^{-12} gm A.Ch. per maximal shock delivered to the preganglionic trunk. In the case of striated muscle, Fleisch, Sibul and Kaelin¹¹ had concluded that the release of A.Ch. was altogether pathological, but in the case of the ganglion I did not consider the evidence sufficient to conclude that even the release of A.Ch. in the small amounts obtained was pathological. At present, however, in view of the results obtained by MacIntosh, it seems probable that some degree of abnormality is always required for the release of A.Ch. in any amount. As this is an important point, a somewhat detailed discussion will be made.

A comparison of the experiments performed by the London school with my own experiments reveals that as technical improvements were introduced in the perfusion of the ganglion, the amounts of A.Ch. released by preganglionic stimulation decreased progressively. In 1934, Feldberg and Vartiainen reported that preganglionic stimulation resulted in the output of 100×10^{-12} to 66×10^{-12} gm of A.Ch. per shock delivered to the preganglionic trunk. But in 1938, by the use of diluted blood as a perfusion fluid, MacIntosh found that in 24 out of 26 stimulations, the output per shock was between 15×10^{-12} and 35×10^{-12} gm, with a mean of 24×10^{-12} gm. In the other two cases the outputs per shock were 8×10^{-12} and 53×10^{-12} gm respectively. In my own early experiments I observed a release of A.Ch. in concentrations so strong that the output per shock must have been as large as, if not larger than the largest figure of Feldberg and Vartiainen. With increasing experience in the preparation of the ganglion, and still using Locke's solution as a perfusion fluid, the concentration of A.Ch. in the output decreased significantly. In experiment XIX,

in which the histological analysis revealed severe damage of the ganglion, the outputs per shock during the first three periods of stimulation respectively were 66×10^{-12} , 58×10^{-12} and 40×10^{-12} gm, i.e., amounts comparable to those reported by Feldberg and Vartiainen. In contrast, in experiments XVIII and XX, in which the subsequently made histological analysis failed to show any significant alteration of the ganglia, the outputs were: Experiment XVIII, 14×10^{-12} , less than 2.3×10^{-12} and 14×10^{-12} gm; and Experiment XX, 4×10^{-12} , 4×10^{-12} and 10×10^{-12} gm, i.e., on the average outputs equal to the minimal output reported by MacIntosh.

For experiments performed with blood-perfused ganglia, Feldberg and Vartiainen reported that preganglionic stimulation causes the release of A.Ch. in concentrations "well within the range of those obtained with the saline effluent of an artificial perfusion." The importance of this finding was emphasized by its being presented as a conclusion: "Preganglionic impulses liberate acetylcholine in the ganglion with natural circulation, as in that artificially perfused." Brown and Feldberg¹² report that in the case of blood-perfused ganglia the concentration of A.Ch. released by continued preganglionic stimulation is maintained almost unchanged, while in the case of ganglia under artificial perfusion the concentration of A.Ch. shows a sharp decline soon after the start of the persistent stimulus. MacIntosh's results were different, because he reports that in blood-perfused ganglia the output of A.Ch., when present, was small, and A.Ch. failed to appear in three out of five experiments. MacIntosh specifically states that in the two positive experiments the concentration of A.Ch. was "well below that found in the perfusion experiments"; and further: "Dr. G. L. Brown informs me that in subsequent experiments of this kind, which he made with Dr. Feldberg in another connection, positive results were not obtained in all cases, in conformity with my own results." MacIntosh also states: "It may, therefore, be regarded as not improbable, that some degree of departure from perfectly normal conditions may be required to enable A.Ch. liberated at the synapses on the ganglion to escape into the circulation so as to be detected in the fluid leaving the vein." In regard to the last statement, however, the present writer believes that if A.Ch. did not escape, even when "it could be shown that the blood contained sufficient eserine to preserve A.Ch.," then there is no proof that A.Ch. was set free outside the synaptic endings to stimulate the ganglion cells.

In some of my experiments it was observed that the passage of impulses through the nodosum ganglion of the vagus resulted in the release of A.Ch. In MacIntosh's experiments this release was not observed.

⁹ W. Feldberg and A. Vartiainen, *op. cit.*

¹⁰ J. H. Gaddum and W. Feldberg, *op. cit.*

¹¹ A. Fleisch, J. Sibul and M. Kaelin, *Arch. Internat. Physiol.*, 44: 24, 1936.

¹² G. L. Brown and W. Feldberg, *Jour. Physiol.*, 88: 275, 1936.

But working with excised vagus nerves and ganglia, Lissák^{13,14} reports a regular release of A.Ch. Apparently, excision creates a greater degree of departure from normal conditions than does perfusion. Be that as it may, Lissák's results lend strong support to my conclusion that the A.Ch. metabolism is a process that is not specific to synaptic junctions.

The results obtained by Lissák may have invalidated my conclusion that entrance into the ganglion cells of impulses conducted in the antidromic direction may result in the release of A.Ch., if the proper conditions for the release have been created. When the postganglionic trunk is stimulated, the escape of the stimulus to the preganglionic trunk is easily prevented, but not escape to the neighboring nerve trunks. Consequently, as the stumps of the X and XII nerves are included in the perfused mass of tissue, the possibility exists that the "antidromic" A.Ch. actually was released by the cut ends of these nerves. This explanation would undoubtedly be adequate, but it would become necessary only if the existence of A.Ch. in ganglion cells should be disproved. Brown and Feldberg¹⁵ report that ganglion cells contain some A.Ch. This statement is denied by Lissák,¹⁶ although Loewi and Hellauer¹⁷ found some A.Ch. in the postganglionic trunk.

Whether the A.Ch. that may be released by preganglionic stimulation is released only, or at least chiefly, at the synapses, has not been demonstrated up to the present time. Direct proof of the synaptic origin was believed to have been obtained in blocking experiments.¹⁸ However, a fundamental, but apparently little known observation of de Castro¹⁹ has demonstrated that nicotine does not paralyze the ganglion cells, but does act on the presynaptic fibers. Therefore, the release of A.Ch. during the nicotine block proves that at least a part of the A.Ch. is released by the presynaptic fibers, and consequently no proof exists that synapses are a more generous source of A.Ch. than the rest of the presynaptic fiber.

Another point under discussion is whether the release of A.Ch., when it does take place, follows the temporal course of synaptic transmission. When using the original technique for the perfusion of the ganglion,^{20,21} in several experiments I found, in agreement with Feldberg and Vartiainen, that A.Ch. was released or its output increased only during the

periods of stimulation of the preganglionic trunk. But later with the use of the new technique I found, this time in agreement with observations made by Barsoum, Gaddum and Khayyal,²² that the output of A.Ch. may considerably outlast stimulation and synaptic transmission. MacIntosh did not observe delayed outputs of A.Ch. and interprets the delayed output in my experiments as a delayed removal of A.Ch. that had been released during stimulation. Without further experimental evidence this question can not be definitively settled; nevertheless, it must be remarked that if the delayed outputs of A.Ch. should have been due to delayed removal, then no significant immediate outputs would have been observed in my experiments, while in fact immediate and delayed outputs were repeatedly observed in the same experiment, the immediate outputs often being the larger.

In conclusion, the fundamental observation of Feldberg and Vartiainen, which has been considered as the direct proof of the chemical theory of synaptic transmission,²³ included several essential points: A.Ch. is released in given amounts at the preganglionic synapses when these are activated by nerve impulses, and the release also takes place in blood-circulated ganglia. The release occurs only at the synapses and only during synaptic transmission. But from later work reviewed in this discussion it appears that A.Ch. is not regularly released by blood-circulated ganglia, but is released only after a certain departure from normal conditions has been created and then in extremely variable amounts. Synaptic transmission is, therefore, possible without the release of any A.Ch., and also with its release in large amounts. The liberation of A.Ch. is a process that is not specific to the synapses and there are experimental results which indicate that it may take place after transmission has been effected. These recently established facts do not diminish the importance of the discovery of A.Ch. metabolism in sympathetic ganglia and other nervous structures. But they make it advisable to consider whether A.Ch., instead of being the synaptic transmitter, actually plays a less specific role in the course of the electrochemical reactions that take place during transmission of nerve impulses and subsequent processes of recovery.

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POSTSCRIPT TO "ROGER BACON WAS MISTAKEN"

My brief article in the March 29 issue of SCIENCE, though needing no modification, would have been much

²² G. S. Barsoum, J. H. Gaddum and N. A. Khayyal, *Jour. Physiol.*, 82: 9, 1934.

²³ H. Dale, "Harvey Lectures," 229 pp., 1936-1937.

¹³ K. Lissák, *Amer. Jour. Physiol.*, 126: 564, 1939.

¹⁴ *Ibid.*, 127: 263, 1939.

¹⁵ G. L. Brown and W. Feldberg, *op. cit.*, p. 265 ff.

¹⁶ K. Lissák, *Amer. Jour. Physiol.*, 127: 263, 1939.

¹⁷ O. Loewi and H. Hellauer, *Pflügers Arch.*, 240: 769, 1938.

¹⁸ H. Dale, *op. cit.*

¹⁹ F. de Castro, *Trav. Lab. Rech. biol., Madrid*, 31: 271, 1936-1937.

²⁰ W. Feldberg and A. Vartiainen, *op. cit.*

²¹ J. H. Gaddum and W. Feldberg, *op. cit.*

more illuminating and valuable had it been prefaced by the following statement of facts.

About 20 years ago a heating engineer told me of his winning \$2 by betting that a pint of boiling water would freeze sooner than a pint of ordinary drinking water if both pints in similar metal vessels were placed outdoors in zero weather. He had successfully tried this experiment several times before and so was guilty of betting on a certainty. Since that phenomenon seemed to me mysterious I tested it at our physics laboratory and got the same result. The mystery disappeared when I weighed the ice and water in the vessel originally hot and found how much less it weighed than the water in the other vessel. The difference was amazing. This will answer the question asked in the last sentence of Professor Sanford's letter. And in the first sentence of his letter he strangely attributes to me a statement entirely different from the one I made.

The experiment which Professor Lyon performed when a schoolboy disgusted his elders, he says, but they erred in concluding that their experience gained through many years was rendered valueless by a single solitary experiment performed by a youngster. His elders knew that when hot-water and cold-water pipes were near each other the hot-water pipes were generally the first to freeze, but they were unaware of the influence of the air contained in the cold water. In experiments like the one I performed Professor Lyon rightly assigns to evaporation the dominant role. In the experiment which disappointed him he used hot water of unstated temperature. My water was 100° hot.

Professor Wakeham and I apparently disagree only in that while he thinks that both the ancients and Roger Bacon were guilty of generalizing I have too much respect for the intelligence of the ancients to believe them capable of teaching that, although boiling water freezes sooner than an equal weight of lukewarm water, the same phenomenon would be observed in case the colder water was only a few degrees above the freezing point. Professor Wakeham's experiments are of great interest and value, and would be of still greater value had he been able to specify not only the minutes but also the approximate number of seconds in each of his observations. His experiment in which the boiling water at 93.3° and the 20-degree water froze in equal times harmonizes entirely with my experiment in which the 100-degree water froze first. For if Professor Wakeham had been able to start with water boiling at 93.3° and an equal weight of 100-degree water, he would have found that when both masses had come to the same temperature, near the freezing point there would have been considerably less of the 100-

degree water than of the other, for in that vessel many more calories had been spent in causing vaporization. Of two unequal masses at the same temperature the smaller freezes first, and consequently Professor Wakeham would have observed the 100-degree water freezing before the 20-degree water just as I did. The 93.3-degree water wasn't quite hot enough to do the trick.

The 2-minute margin of victory of the 10-degree water over the 93.3-degree would have been considerably narrowed, perhaps obliterated, had 100-degree water been at Professor Wakeham's disposal; but a victory should surprise no one, as will appear from the following considerations. As long ago as 1889 Professor Tyndall wrote, "This halt in contraction of the approaching molecules at the temperature of 39° F. (about 4° C.) is but a preparation for the subsequent act of crystallization." Further, it should be kept in mind that water is highly polymerized, a compound of H_2O , $2H_2O$ and $3H_2O$ and that the ratio of these polymers changes with the changes in temperature. According to Rao (1933) 59 per cent. of ice at 0° is composed of $3H_2O$. Also many ice crystals exist in water from 0° to 10° and beyond. With all these advantages it is not surprising that 10-degree water freezes sooner than water boiling at 93.3°.

From the above facts it is clear that not only was the writer of the book from which I quoted ill-advised in denouncing as "drivel" the findings of the ancients, but also that, even ignoring considerations of courtesy in saying "the ancient author was a liar," Roger Bacon was mistaken.

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AMHERST COLLEGE

A COUNTER-STATEMENT

THE statement that follows has been approved by those whose names appear as signers.

In *SCIENCE* for May 3, 1940, there appears an appeal for signatures to a peace manifesto sponsored by the American Association of Scientific Workers. It seems desirable to put on record the fact that this statement does not represent the unanimous opinion of American scientific workers.

One may question whether the manifesto will represent the considered opinion of all its signers, for a casual reading of it might easily fail to disclose its real implications.

It is a platitude that all right-thinking people are, in general, in favor of peace—and the fact is not worth troubling to specify for scientific workers in particular. To lay emphasis on the point now can only be interpreted as implying that in the opinion of the signers our only concern is the re-establishment of peace, regardless of the terms on which it is based.

The manifesto lays emphasis on the importance of the United States keeping out of the war in order to insure

the continuation of intellectual progress. Intellectual matters know no national boundaries, and a purely national culture must be a poor thing indeed. The primary concern of any intelligent person must be the establishment and preservation of intellectual freedom and intellectual activity in the world as a whole. In a large part of the world these things have already been suppressed and in another part they are now in serious danger. If this country announces that under no circumstances will it take an active part in the struggle the sole effect will be to encourage the forces opposed to democracy and freedom of thought.

It might have been supposed that proponents of "peace at any price" would have been silenced by the proof that peace alone is not enough to insure intellectual freedom (as in Russia and Germany), and by what has happened to such peace-loving countries as Czecho-Slovakia, Finland, Denmark and Norway.

I. W. Bailey, Harvard University

James Bonner, California Institute of Technology

Robert Chambers, New York University

Alfred E. Cohn, Rockefeller Institute
W. J. Crozier, Harvard University
Hallowell Davis, Harvard University
Th. Dobzhansky, California Institute of Technology
Sterling Emerson, California Institute of Technology
Alexander Forbes, Harvard University
Ernst A. Hauser, Massachusetts Institute of Technology
Hope Hibbard, Oberlin College
Leigh Hoadley, Harvard University
Hudson Hoagland, Clark University
T. H. Morgan, California Institute of Technology
Linus Pauling, California Institute of Technology
Peyton Rous, Rockefeller Institute
Karl Sax, Harvard University
A. H. Sturtevant, California Institute of Technology
Albert Tyler, California Institute of Technology
R. H. Wetmore, Harvard University

From the responses obtained it is clear that, had more time been available, a much longer list of signatures could have been secured.

A. H. STURTEVANT

SCIENTIFIC BOOKS

EMBRYOLOGY

The Rise of Embryology. By ARTHUR WILLIAM MEYER. Stanford University, Stanford University Press. 1939. xv + 367 pp., 97 figs. \$6.00.

IN his new work, "The Rise of Embryology," Professor Meyer has chosen wisely to present "the history of the basic ideas in embryology," and wisely too, in the reviewer's opinion, has quoted liberally from the original sources, often in his own translations, "to avoid misinterpretation and to indicate something of the intellectual atmosphere of the time." The author has sought to efface his personal views, "for they are of the day," and "to reveal facts, not to utter dicta." The treatment throughout is sympathetic, for Dr. Meyer has a commendable understanding of the difficulties under which the early workers strove, and it reveals an unusually wide acquaintance with the sources, a fact to which the excellent bibliography of 19 pages abundantly testifies. In most cases the author brings his account down to the first quarter or half of the nineteenth century.

The first chapter deals with "Aboriginal Ideas of Reproduction," the beliefs of primitive peoples. Chapter II, "Early Historic Ideas of Reproduction," presents in the briefest possible way some of the more important views of the civilized peoples of antiquity, and especially those of Greece. There follows an interesting chapter on the tenacious doctrine of spontaneous generation which reached the height of absurdity, and, perhaps charlatanry, in Paracelsus. Chapter IV traces the history of the doctrine of epigenesis to von Baer's

day. The author quotes the "New English Dictionary," which ascribes the first use of the word "epigenesis" to the year 1807. However, the reviewer finds the term used as an English word in the 1653 translation of Harvey's "De generatione animalium" (e.g., Ex. XLV, p. 224). The treatment of the preformation theory in Chapter V is excellent, and this is followed by brief but adequate discussions of "Pangenesis," and "Panspermism or Panspermatism" in Chapters VI and VII. Chapter VIII presents the absorbing story of "The Search for the Mammalian Ovum." On p. 100 Fabricius is said to have recognized "three parts in the uterus of the hen: (1) the ovary, and (2) the superior and (3) the inferior portions of the oviduct, which he included in the uterus." More correctly, the "superior uterus" of Fabricius is the ovary, the "inferior uterus," the entire oviduct; the latter Fabricius divides into three portions. On the same page Adelman is incorrectly stated to have said that Coiter "noticed the openings in the ruptured ovarian vesicles," etc. That statement was made about De Graaf (see *Annals of Med. Hist.*, N. S., 5: 338-339). Coiter does not mention the rupture of the Graafian vesicles, but on p. 140 Dr. Meyer says he does. The statement that "to both Harvey and Fabricius the ovum was the beginning of the development of any animal" (p. 101) is incorrect as applied to Fabricius, nor is it true that "both Fabricius and Fallopius expressed the idea that viviparous animals may arise from egg-like primordia" (p. 128). Certainly Fabricius never speaks of the "conception" of the vivipara as an egg, or even as "egg-like." Dr. Meyer has apparently been misled by a

statement of Harvey to that effect. Where does Fallopius express such an idea? On p. 104 Dr. Meyer says, "It will be recalled that Fabricius already had suggested the word *ovarium* for the *testes mulibre* (*sic!*) but the suggestion apparently received very little attention until 1667, when Nicolaus Steno also made it, unaware of the fact that Swammerdam and De Graaf both had done so three years previously." That statement is misleading. Fabricius applied the term *ovarium* to the ovary of ovipara, not to the *testis muliebris*, the ovary of viviparous animals, which he calls a *testis muliebris* or sometimes a *glandula*. The latter term apparently inspired Harvey to speak of the mammalian ovaries as *quasi parvae glandulae*. Further, is there any evidence that either Swammerdam or De Graaf published such an idea in 1664? Dr. Meyer, one suspects, is thinking of Swammerdam's claim that he and van Horne had independently come to the same conclusion as Steno, apparently in 1666 or 1667.

The last paragraph on p. 128 gives the impression that all von Baer's "Entwicklungsgeschichte" was translated into French by Breschet. Actually, only pp. 3-140 of Part I were translated.

The last paragraph on p. 130 is confusing. Von Baer makes quite clear his reason for stating that Purkinje's vesicle is absent in the eggs of hens kept without a rooster. He rejects Purkinje's idea that the disappearance of the germinal vesicle in the oviduct is due to pressure exerted by contraction of the infundibulum and then inquires whether its disappearance may not be due to fertilization. He decides that fertilization can not be responsible because he has found that in hens kept without a cock the Purkinjean vesicle is absent in eggs which are passing through the oviduct. Hence, von Baer concludes that the vesicle is expelled from the egg before fertilization and that it is dissolved between the yolk and vitelline membrane.

The "Discovery, Origin, and Meaning of the Spermatozoon" is the subject of Chapter IX, which is followed by a discussion of "Changing Ideas of Impregnation or Fertilization." The salient facts are ably presented. The statement on p. 159, "Aristotle thought that eggs can be impregnated twice—first in the ovary, and again after they leave it"—is, however, misleading, for Aristotle had no clear conception of the ovary and oviduct of the fowl nor of their respective roles in the production of an egg. Aristotle merely says, "Wind-eggs can turn into fertile eggs, and eggs due to previous copulation change breed, if before the change of the yellow to the white the hen . . . be trodden by another bird. (*Hist. An.*, VI, 2).

"The Role of the Mule" is the alluring title of Chapter XI, which treats of hybrids, but carries the subject no further than the end of the 18th century. "The Problem of Malformation" is presented in Chap-

ter XII. One wonders why Colombo is emphasized as one of those who contributed facts leading to a more rational view of abnormal development. Chapter XIII tells many interesting facts about the development of the microscope and other technical aids in preparation for a discussion of "The Growth of Morphology" in Chapter XIV. The treatment of the latter is perforce brief and uneven.

Aristotle, Herophilus and Leonardo da Vinci are lightly touched upon. Alessandro Benedetti is said to have examined a pregnant bitch; but Benedetti opened the deer's uterus—"cervinum uterum olim resecamus," *Hist. corp. Hum.*, Lib. II, cap. 23).

The accounts of Coiter and Aldrovandus are too brief to be informative. Dr. Meyer quotes Needham's statement that Aldrovandus "was the first biologist since Aristotle to open the eggs of hens regularly," etc. Perhaps so, but we must remember that his work did not appear in print until 1600, twenty-eight years after Coiter's work was published, and that there is no real evidence to prove that Coiter did not actually make his study before Aldrovandus, even though his teacher stimulated him to do so. On p. 296 Coiter is listed as one of the men who made "good and abundant use" of illustrations. It should be remembered, however, that Coiter did not illustrate the development of the chick.

Spigelius also has been treated too briefly. His "De formato foetu" first appeared at Padua in 1626, not "in Frankfurt in 1631." Even though Vesalius's faked illustration in the 1555 edition of his "Fabrica" induced Spigelius to say that the human foetus has an allantois, it is not surprising to find that the allantois does not appear in the illustrations Spigelius borrowed from Casserius, because the foetuses illustrated are all at or near term. Further, Spigelius did not neglect to give an explanation of the *cutis sordes* [*vernix caseosa*]. He says that it protects the skin from the deleterious effects of the sweat in the amnion and prevents the outflow of vital spirits through the pores of the foetal skin, which are more open than after birth.

Hieronymus Fabricius ab Aquapendente is considered at length, and four extracts from his "De formatione ovi et pulli" are presented in translation. The emphasis is placed on Fabricius' statement that the chick arises from the chalaza, not from the cicatrix. One wishes, however, that some constructive aspect of his work had been stressed—his real contribution to the knowledge of placental structure, for example.

It is doubtful if an edition of Fabricius' "De formato foetu" was ever issued in 1600, as Dr. Meyer says.

"The nucleus of the unfertilized hen egg," says Dr. Meyer, "is large and conspicuous." What does he mean? The reviewer would emend a number of Dr. Meyer's renderings in the extracts from Fabricius,

e.g., on p. 285, line 14, for "from the substance," read, "by the substance"; in line 17, for "Indian hen," read, "turkey hen"; line 29-30, for "or that something . . . eggs," read, "or that something analogous (to the chalazae) has been laid down, as in the smallest eggs" (*aut analogon quid esse positum, ut in minimis ovis*); line 34, *turrita* is probably the wild pigeon; line 38-p. 285, line 1, for "that all agree . . . eggs," read, "that it is reasonable to believe that chalazae are present in all eggs; line 1, for "I exclude," read, "I have refrained from observing"; line 9, for "two," read, "too." Dr. Meyer says on p. 287 that Fabricius believed that the seminal material of "vipera" is slight in quantity; Fabricius makes that statement of vivipara.

Harvey receives somewhat briefer treatment than Fabricius. Highmore is mentioned briefly, and Descartes is justly reprimanded for having "set a bad example, indeed, for men of science" by his "loose generalizations." Walther Needham, Malpighi, Kerkering, Kuhlmann and Haller pass in review, and then comes a splendid, extensive account of John Hunter's work on the development of the goose egg. Caspar

Friedrich Wolff's, von Baer's and Purkinje's contributions form a fitting climax.

In the last chapter the author cites a number of interesting facts to support his contention that "Experimentation—is not the child of to-day," and to disprove the statement that "until 1859 embryologists were content to follow changes in form."

The book is illustrated by 97 figures, admirably selected, but in some instances indifferently reproduced. Fig. 91, taken from Plate VIII of Pander's "Beiträge zur Entwicklungsgeschichte," etc., has unfortunately been reversed by the printer, and the legend attributes it to von Baer. The few typographical misprints are of no serious consequence, neither is the omission of a few works from the bibliography.

While the more important slips of the pen have been pointed out, it should be emphasized that they do not seriously impair the value or importance of Dr. Meyer's fine book. It is a work which supplements admirably Needham's "History of Embryology"; this reviewer welcomes its appearance.

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SPECIAL ARTICLES

ALCOHOL TASTE THRESHOLDS AND CONCENTRATIONS OF SOLUTION PREFERRED BY RATS

In a previous study¹ it was found that rats whose only access to fluid was in the form of an 8 per cent. alcohol solution drank the same total volume as a control group of rats which had access only to tap water. No abnormal behavior was observed and the rate of growth and the activity curves were the same. The experimental animals reduced their food intake, as measured in calories, in proportion to the caloric value of ingested alcohol, thereby maintaining a caloric value equal to the number of calories ingested by control rats on the standard diet. It was further reported that rats restricted in fluid to a 16 per cent. solution of alcohol differed from the 8 per cent. group only by slightly decreased activity and a reduced total volume of fluid intake. The animals refused to take more alcohol in grams than the first group obtained from the 8 per cent. solution. The fact that the rate of growth and activity curves were normal for many months when the alcohol replaced from one fourth to one third of the stock diet demonstrated that alcohol served as a food.

Since publication of the above study on alcohol, numerous instances of beneficial regulatory activities of rats have been reported. Thus, it was found that adrenalectomized rats maintained a constant internal

salt environment and kept themselves alive by ingesting large amounts of salt;² similarly, parathyroidectomized rats ingested large amounts of calcium solution and thus kept themselves free from tetany.³ Rats even make beneficial selections when allowed to select their entire diet from purified (or nearly purified) substances.⁴

Using a technique originally devised to determine the taste thresholds of rats for such substances as salt,⁵ sugars,⁶ etc., we have obtained further information regarding the ability of rats to regulate their alcohol intake. These results throw more light also on the nutritional value of alcohol. In these experiments the rats, kept on our standard McCollum diet, had access for several weeks to two graduated bottles filled with distilled water. Intake from each bottle was recorded daily. When the intake from each bottle had reached a fairly constant level, we put a subliminal concentration of alcohol solution (0.01 per cent. by weight) in one bottle. Thereafter each day we increased the concentration in small steps. Fig. 1 gives the record of one of the animals. The ordinates indicate fluid intake in cubic centimeters; the abscissae

² Curt P. Richter, *Am. Jour. Physiol.*, 115: 155, 1936.

³ Curt P. Richter and John F. Eckert, *Endocrinology*, 21: 50, 1937.

⁴ Curt P. Richter, L. Emmett Holt, Jr., and Bruno Barelare, Jr., *Am. Jour. Physiol.*, 122: 734, 1938.

⁵ Curt P. Richter, *Endocrinology*, 24: 367, 1939.

⁶ Curt P. Richter and Kathryn H. Campbell, *Am. Jour. Physiol.*, 128: 291, 1940.

¹ Curt P. Richter, *Jour. Exp. Zool.*, 44: 387, 1926.

indicate time in days, and also the concentrations of the alcohol solutions offered each day. The record does not show the 10-day preliminary period during which

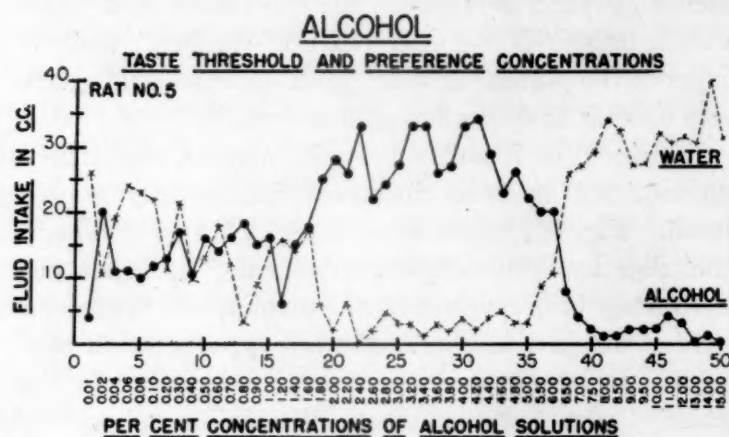


FIG. 1.

both bottles were filled with distilled water. For the first 18 days, when the concentrations increased from 0.01 per cent. to 1.4 per cent., the rat drank almost equal amounts of distilled water and of the alcohol solution. However, it showed a preference for the 1.8 per cent. and for all concentrations up to 4.8 per cent. It drank large amounts of these solutions and small amounts of water. It showed its greatest preference for alcohol solutions from 2.4 per cent. to 4.4 per cent. With higher concentrations its preference decreased. It still showed a slight preference for the 6.0 per cent. alcohol solution, but preferred distilled water to alcohol solutions in all higher concentrations. It drank only minimal amounts of any alcohol solution above 7.0 per cent. Thirteen out of seventeen rats had similar records; three never manifested a preference for alcohol; one preferred water to the alcohol.

The results of some of our previous experiments may throw some light on the significance of these results. Thus far we have found that rats showed preferences for certain concentrations of solutions of substances, such as glucose, maltose, sucrose, galactose, sodium chloride, potassium chloride and dibasic sodium phosphate, all of which are known to play an important part in nutrition. The rats preferred distilled water to poisonous substances, such as mercuric chloride, arsenic trioxide and morphine sulfate, even when offered in extremely low concentrations. These experiments demonstrate that, according to the rats' appetite, alcohol belongs to the group of substances that play a part in normal nutrition.

Further experiments are in progress to determine the effects produced on alcohol taste threshold and maximum preference concentrations by removal of the olfactory bulbs, surgically induced brain lesions, dietary deficiencies, glandular deficiencies and forced alcohol feeding over long periods of time. After long forced alcohol feeding will rats have a higher or lower threshold for alcohol and will they prefer alcohol to

water in concentrations above 6 per cent.? This might give a quantitative measure of any addiction to alcohol.

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THE SYNTHESIS OF NICOTINIC ACID IN THE BODY OF SHEEP¹

ON the basis of growth, evidence² has been presented indicating that nicotinic acid is not a dietary essential for sheep. It has recently been shown that dogs restricted to a typical blacktongue-producing diet after about 28 days virtually cease to excrete nicotinic acid in the urine.³ Rats remain free from deficiency disease when restricted to a diet that is deficient in nicotinic acid only. They continue, however, to excrete appreciable amounts of nicotinic acid in the urine even after being on the deficient diet for long periods of time.³

Since species which require nicotinic acid cease to excrete it when on a deficient diet, its occurrence in the urine of animals restricted to such a diet indicates that it is synthesized in the body. Lambs approximately 3 months of age were placed on a nicotinic acid-deficient diet consisting of regenerated cellulose 20, brewer's rice 49.5, purified casein 9, corn 16, cow peas 2.5, salts mixture 3 and oleum percomorphum weekly to furnish vitamins A and D. Dogs fed this diet, with the modification that the cellulose was omitted, showed a marked decrease in their urinary nicotinic acid and developed typical blacktongue symptoms. After the lambs had been on the experimental diet approximately 8 months the urine was collected for the estimation of nicotinic acid. The nicotinic acid was determined photometrically on unhydrolyzed samples of urine by the cyanogen bromide-aniline reaction.

The figures in the table for the urinary excretion of

Number	Diet	Total per day	Per kg. wt. per day
		mg	mg
418	Deficient	2.52	0.13
420	"	5.33	0.39
488	"	2.81	0.12
443	"	1.95	0.08
443	Deficient + 1 mg n.a./kg wt./day for 13 days	2.86	0.12
443	Deficient + 2 mg n.a./kg wt./day for 5 days	3.00	0.13
443	Deficient + 4 mg n.a./kg wt./day for 13 days	5.16	0.22
3261	Alfalfa hay and grain	2.76	0.09
3439	" " " "	5.74	0.21
523	" " " "	3.23	0.14

¹ Published with the approval of the director of the Texas Agricultural Experiment Station as Technical Contribution No. 592.

² P. B. Pearson, H. Schmidt and A. K. Mackey, *Proc. Soc. Exp. Biol. and Med.*, 40: 423, 1939.

³ L. J. Harris and W. D. Raymond, *Biochem. Jour.*, 33: 2037, 1939.

nicotinic acid by sheep on various regimens are average values for 3 consecutive 24-hour collections. While there is considerable variation in the amount of nicotinic acid excreted in the urine the level is not essentially different, irrespective of whether or not the diet is deficient. Supplementing the deficient diet with nicotinic acid augmented the excretion. The most probable explanation of the continued excretion of nicotinic acid by sheep on a diet deficient in this constituent is that this species can synthesize it either in its tissues or it is formed in the rumen by microorganisms, a process analogous to the synthesis of thiamin, riboflavin, B₆, and pantothenic acid.⁴

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BREAKDOWN OF SULFANILAMIDE MOLECULE BY ULTRA-VIOLET IRRADIATION OR CHEMICAL OXIDATION

In the course of some experiments with ultra-violet irradiation it was observed that dilute aqueous solutions of sulfanilamide became more acid (glass electrode or methyl red as pH indicator). This was taken as an indication of oxidation of the sulfonamide group with liberation of acid sulfur radicals. Proof of a breakdown of the molecule was obtained in that irradiated solutions showed the presence of ammonia by reacting strongly to Nessler's reagent, and of inorganic sulfur by giving a precipitate with barium chloride in acid solution. That the free amino group is also affected has been previously shown by Ottenberg and Fox¹ by a decrease in the diazo reaction under such conditions. By the use of light filters the most effective wave lengths were found to be below 270 mμ, the same region of the spectrum shown by Fox² to bring about the colored products.

The amount of sulfur split off was a function of the length of irradiation. When aqueous solutions of sulfanilamide containing 40 mg per cent. were irradi-

ated by a Hanovia Mercury Arc Lamp at 20 cm distance for 2, 4, 8 and 16 minutes the amounts of sulfur split off were 8.6, 16.1, 29.1 and 40.8 per cent., respectively, of the total amounts present. Varying the concentration of sulfanilamide from 20 to 100 mg per cent. caused only slight variations in the total amounts of inorganic sulfur recovered after a uniform exposure of 10 minutes.

Irradiation of the ortho and meta isomers of sulfanilamide, of acetyl sulfanilamide and of sulfanilic acid for 10 minutes under the above condition did not bring about similar changes, except for the liberation of some ammonia with sulfanilic acid.

Oxidation of sulfanilamide by chemical agents has been carried out by Shaffer³ whose attention was directed to the amino group. Preliminary experiments have shown that the oxidation of dilute aqueous solutions by ferric chloride and hydrogen peroxide is also attended by the liberation of ammonia and inorganic sulfur. The amount of sulfur split off was likewise dependent upon the amount of iron added, indicating that the process is not a catalytic reaction.

After standing at room temperature for 18 hours, 400 cc of an aqueous solution containing 100 mg of sulfanilamide, 2.2 mg FeCl₃ and 0.5 cc 3 per cent. H₂O₂ showed 15.7 per cent. of sulfur split off. Under similar conditions the ortho isomer showed 9.7 per cent., the meta isomer 4.8 per cent. and sulfanilic acid (neutralized) 18.3 per cent. of sulfur split off. These results are not comparable to those with irradiation, which was applied for only 10 minutes.

Because of the irreversible nature of these changes it is obvious that potentiometric studies of such solutions are not valid. Whether or not the body is capable of splitting off any of the sulfonamide group remains to be demonstrated. The demonstration by James⁴ of p-aminophenol in the urine following sulfanilamide therapy is evidence to this effect.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

A SPEEDIER AND LESS COSTLY METHOD OF CONCENTRATION IN NITRO-CELLULOSE IMBEDDING

In the hot nitrocellulose method of imbedding histological and cytological material as developed by

⁴ L. W. McElroy and H. Goss, *Jour. Biol. Chem.*, 130: 37, 1939.

¹ R. Ottenberg and C. L. Fox, Jr., *Proc. Soc. Exper. Biol. and Med.*, 38: 479, 1938.

² C. L. Fox, Jr., J. E. Cline and R. Ottenberg, *Jour. Pharm. and Exper. Therap.*, 66: 99, 1939.

Jeffrey,¹ and somewhat elaborated by Wetmore,² chips of celloidin in small metal troughs are used to absorb the ether and alcohol and thus concentrate the liquid in which the material is being imbedded. Around any laboratory using this process a certain amount of used celloidin soon accumulates. It often contains particles of imbedded material as well as dirt from containers

³ P. A. Shaffer, *SCIENCE*, 89: 547, 1939.

⁴ G. V. James, *Biochem. Jour.*, 33: 1688, 1939.

¹ E. C. Jeffrey, *Bot. Gaz.*, 86: 456-467.

² R. H. Wetmore, *Stain Tech.*, 7: 37-62.

and tables. The author has found that when this is redissolved in the usual ether-alcohol solvent and allowed to stand for a week or so, almost all of the refuse will sink to the bottom of the jar. The nitrocellulose may then be poured into petri dishes to a depth of a quarter of an inch. A little chloroform poured on top will aid in the solidification which should proceed until the celloidin is dry enough to cut with the shears or a razor. Cut into squares of approximately an inch, gather these on a No. 1 or longer pin, and allow to dry completely. These may then be used in place of the troughs in the position as shown in Fig. 1. The use of a pin diminishes the chance of pro-

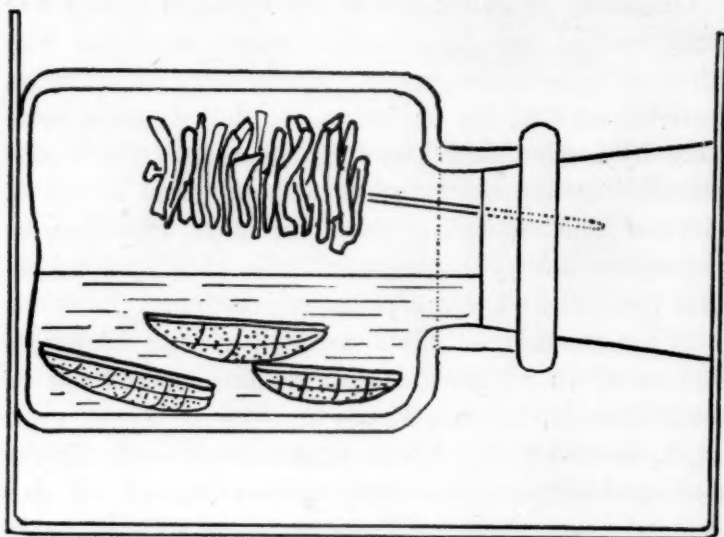


FIG. 1.

ducing a leaky cork after several changes and with the increase of absorbing surface the time required to concentrate the 10 per cent. celloidin is shortened by several days. This is also dependent upon the number of times the pins are changed each day; usually twice being sufficient. If mounted material is placed in the bottles with the cardboard side up and if the oven shelf is raised a bit in front, the hazard of finding some of the material sticking out of the celloidin is much reduced. For most cytological material the nitrocellulose series may also be cut down to changes of 2, 6 and 10 per cent. without any apparent damage to the material. The above recommendations reduce the time factor which some investigators find objectionable in a method of imbedding which is otherwise quite superior to paraffin.

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AN INEXPENSIVE MICROPHOTOGRAPHIC CAMERA

A "UNIVEX" Camera, Model A F, which costs but \$1.00, can be adapted for the filming of microscopic objects with little trouble and less mechanical skill. This camera is provided with instantaneous and time settings on its shutter. In order to use it in conjunc-

tion with a microscope, one has merely to remove the lens of the camera. This is done by setting the shutter for "time" and opening it. A nail is held against the lens and is then struck a smart blow with a small hammer. The lens is easily shattered, and the pieces can be shaken out.

The wire frame that is normally used as a finder is drawn out and the middle (horizontal) section is removed by bending the angles a few times. The two side pieces are then bent down along the front of the lens board and then curved slightly to receive the eye-piece of the microscope. The two wires are held together by means of a loop of wire passed around them just above the eye-piece.

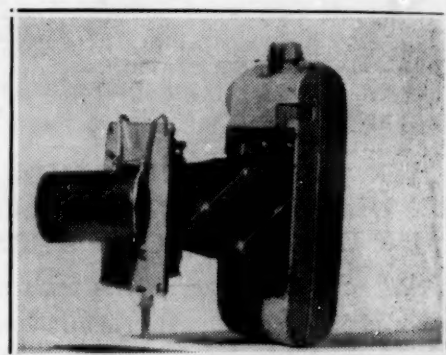


FIG. 1

An eye-piece is clipped to the camera and then placed in the microscope. In order to focus the camera, a piece of ground glass or tracing paper 33 x 45 mm is placed over the opening of the camera with the back removed. The roll of film, which costs but 10 cents, is placed in the camera and six exposures are made with varying times. At least one of the exposures will give a sharp negative which can be printed directly or enlarged many times since the grain is very fine.

No rules for exposure can be given since that depends so much on the illumination.

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